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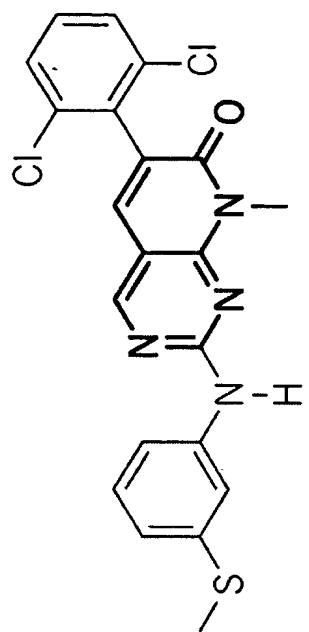
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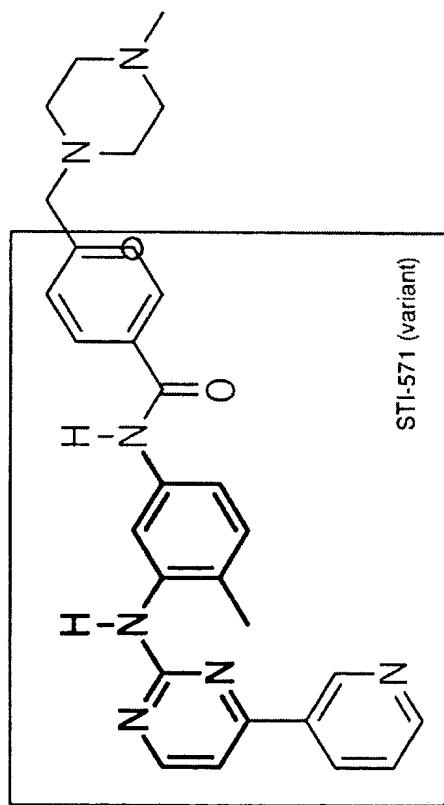
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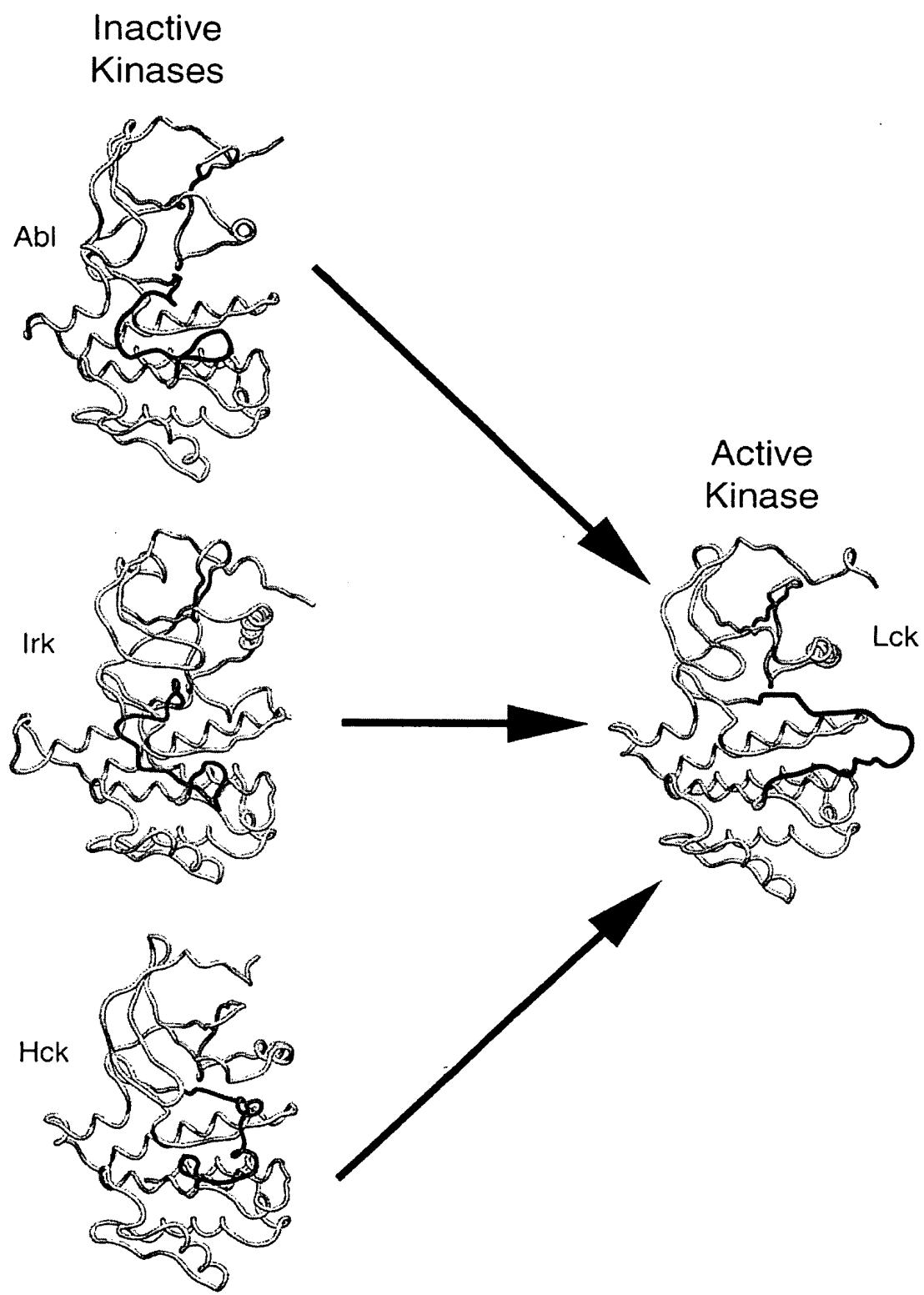


PD173955

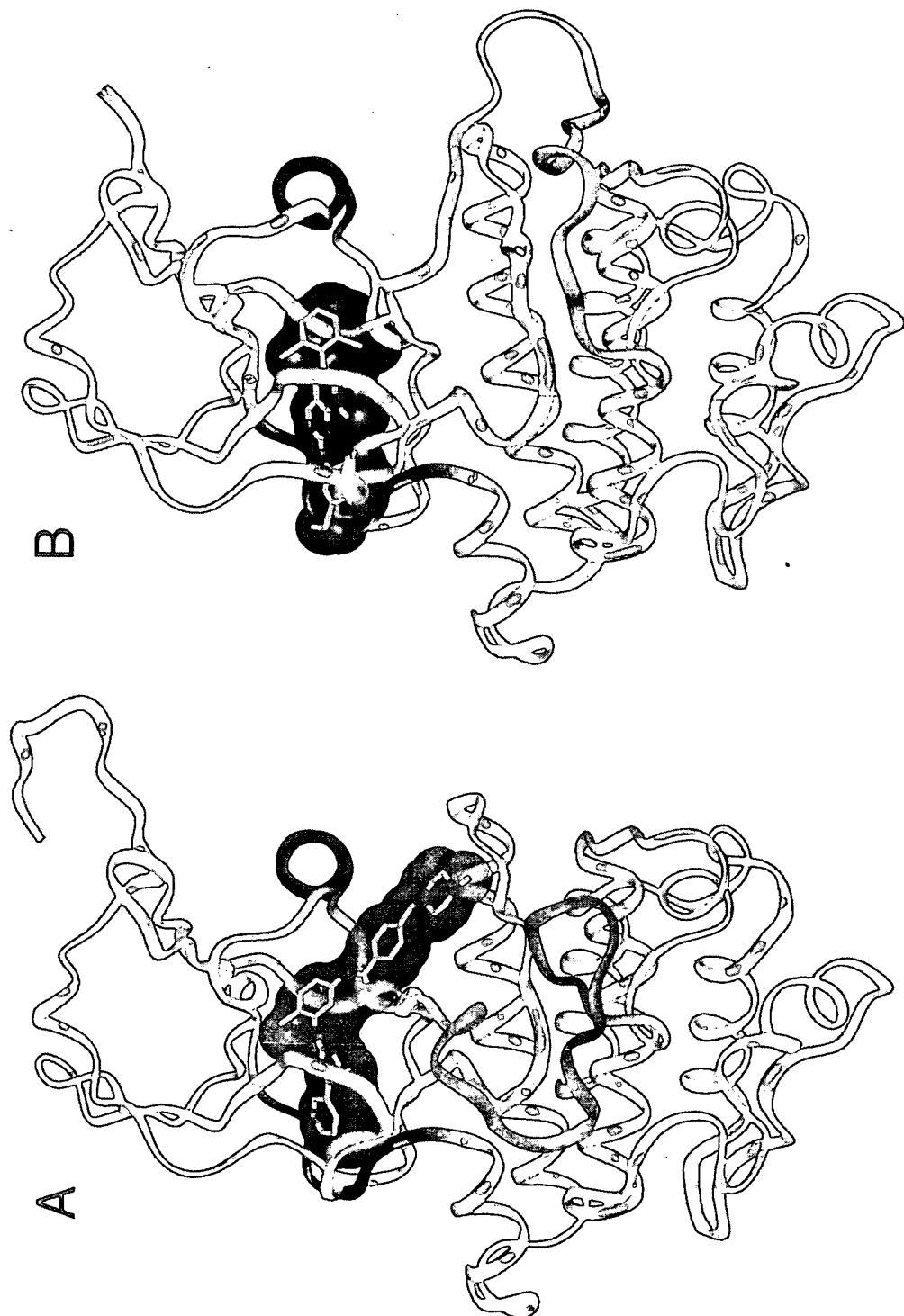


STI-571

Figure 1

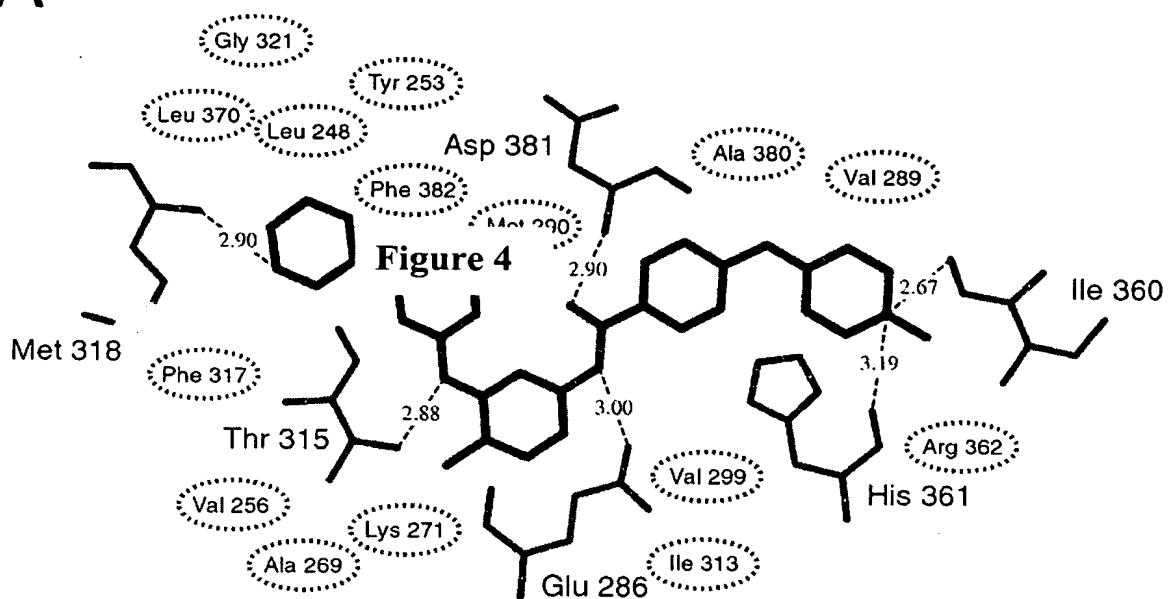


**Figure 2**

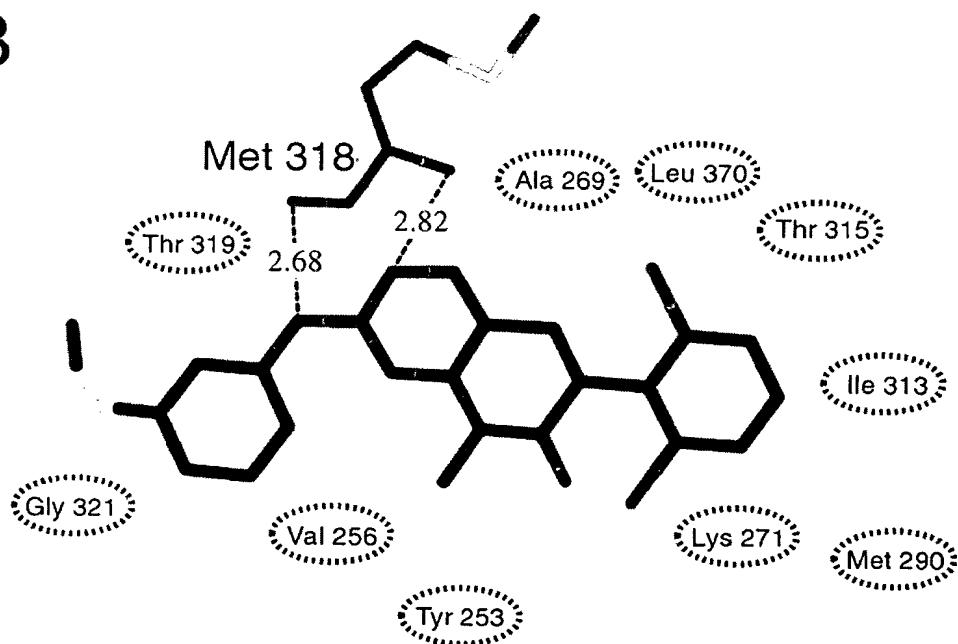


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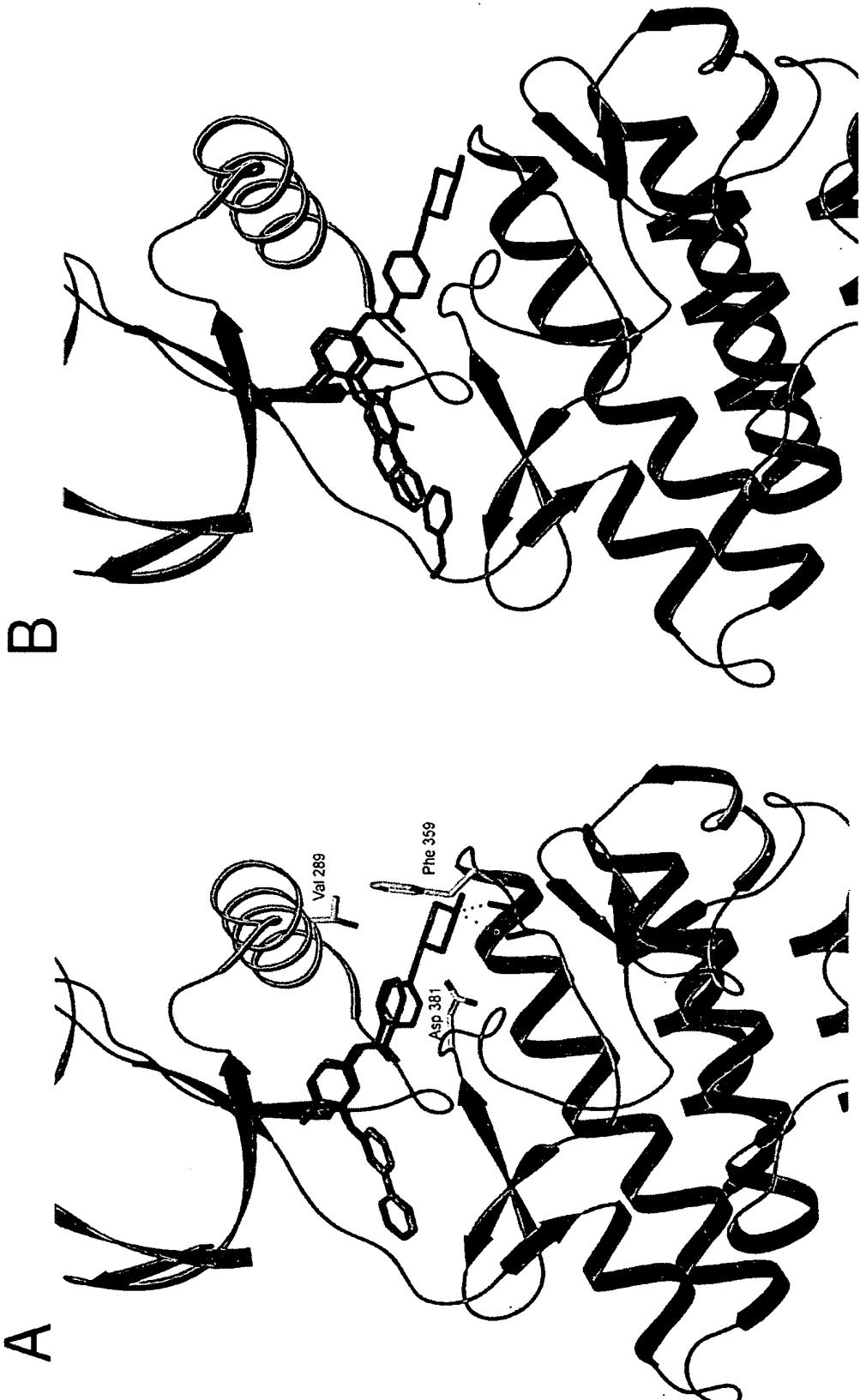
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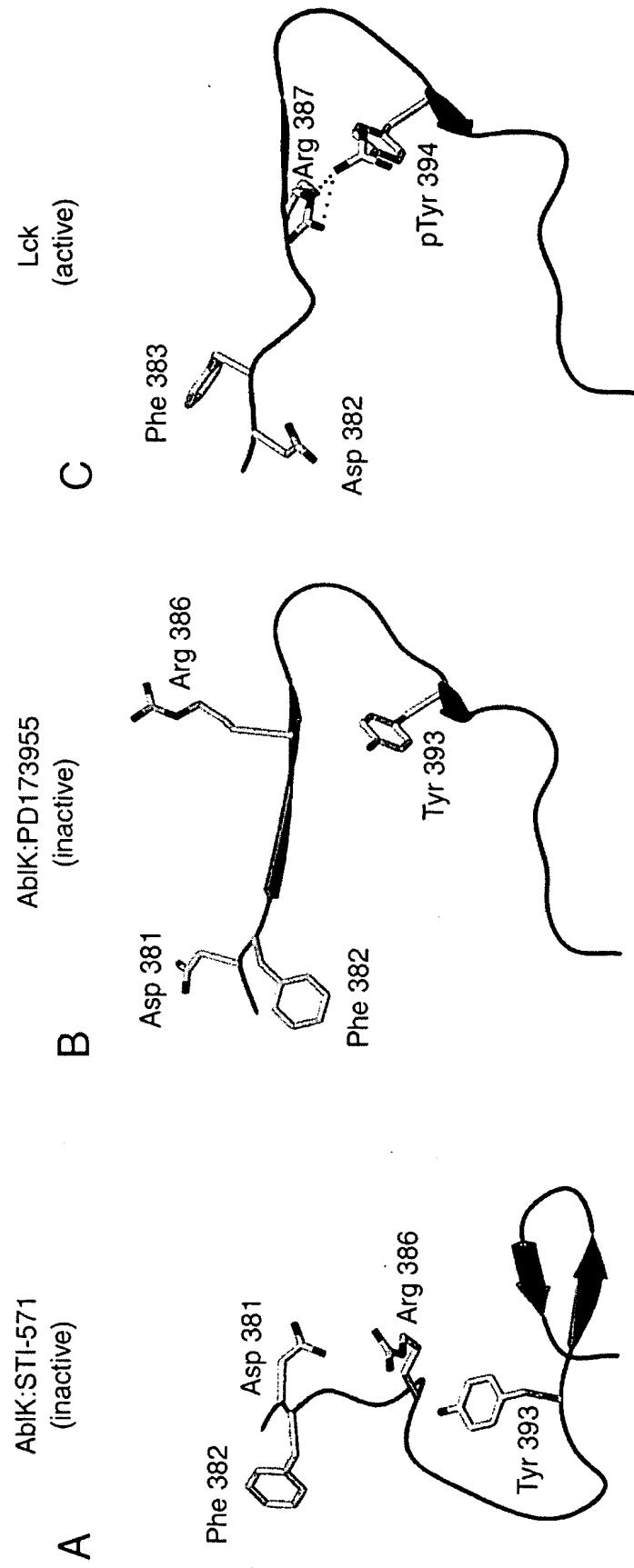
B



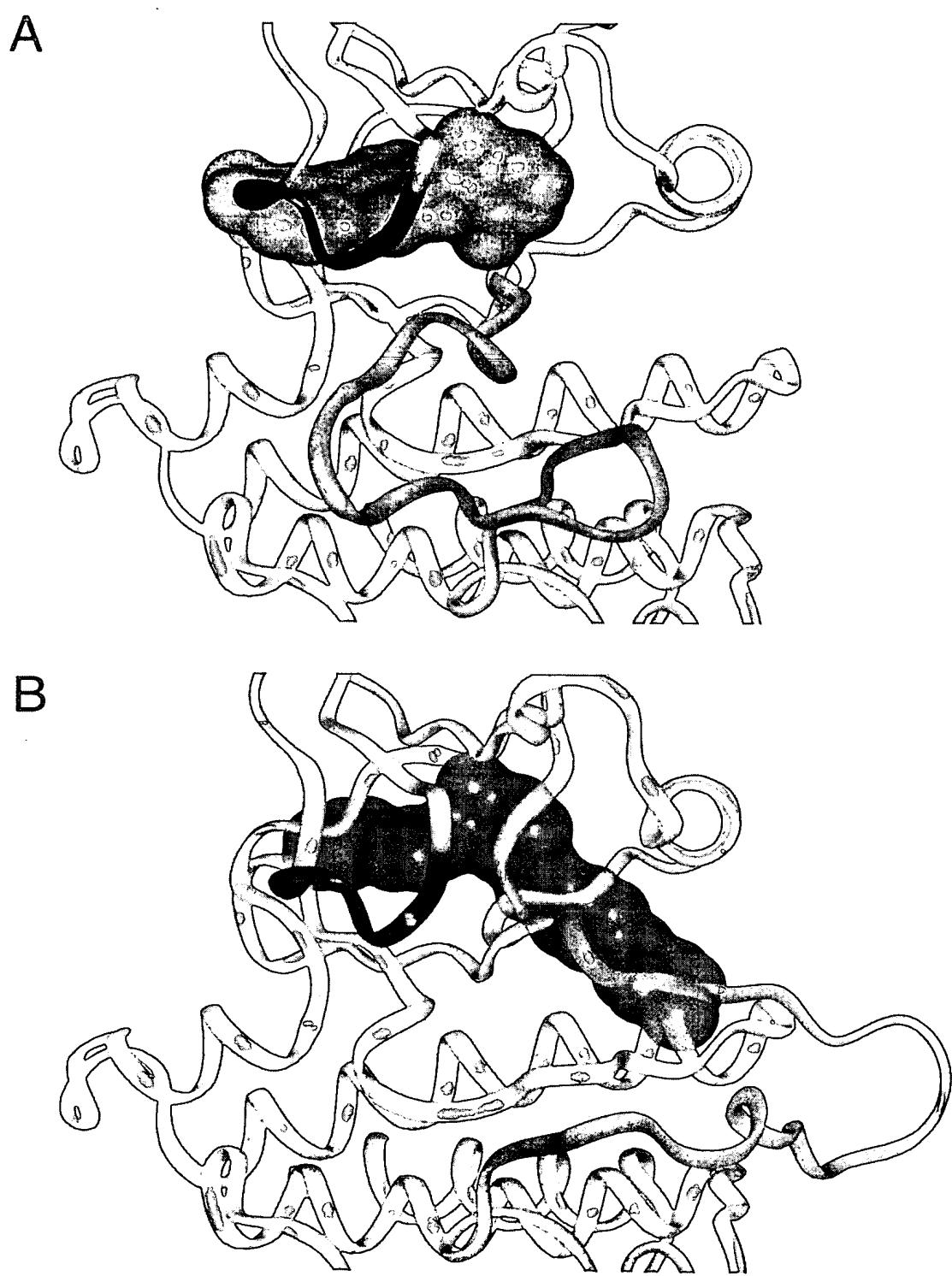
**Figure 4**



**Figure 5**

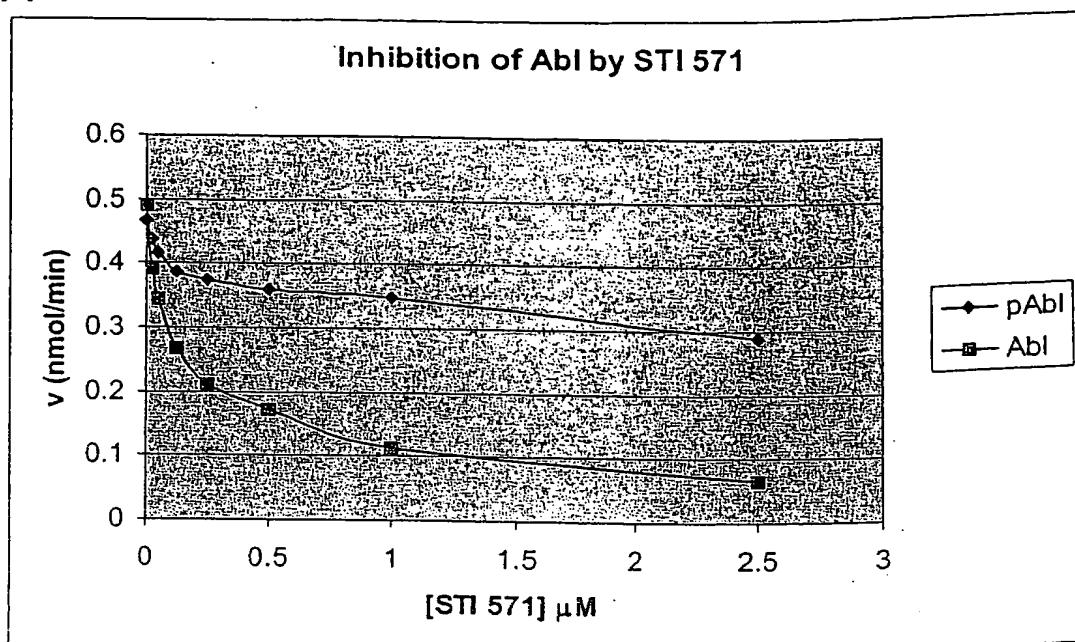


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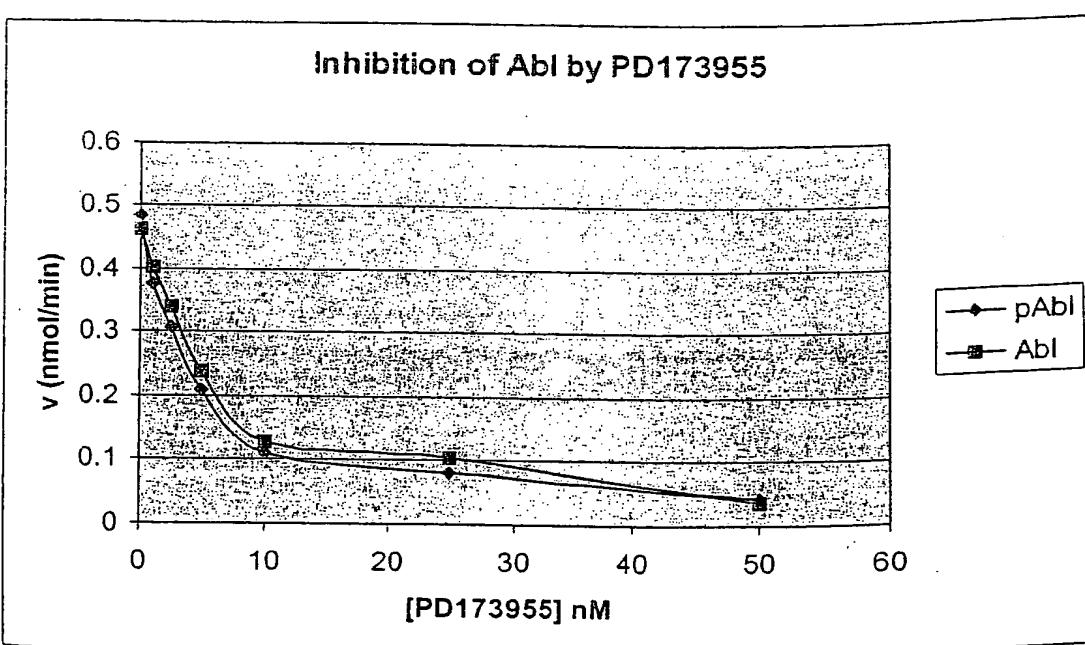


**Figure 7**

A

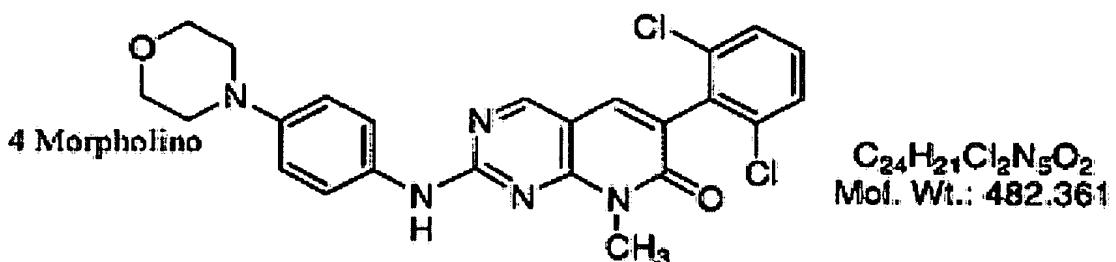


B

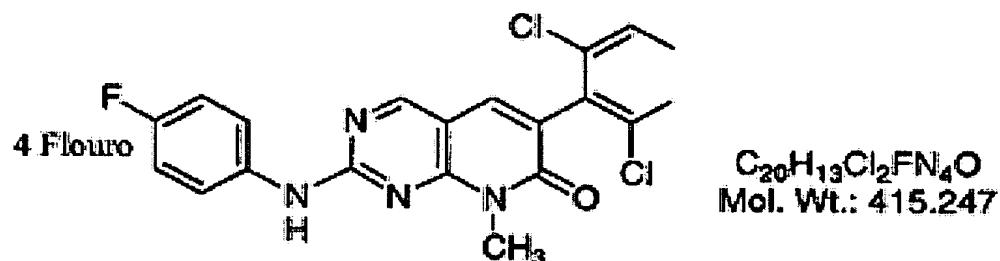


**Figure 8**

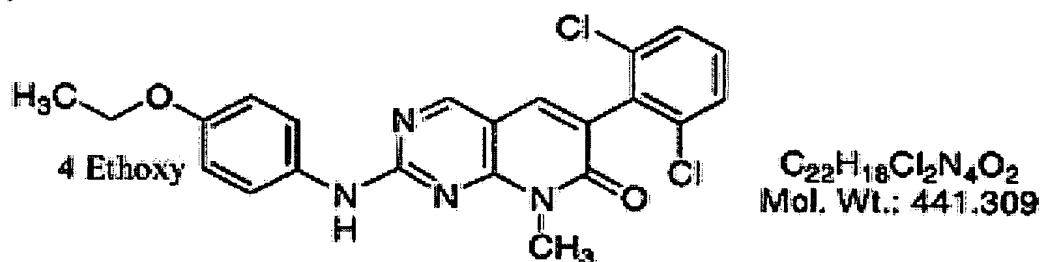
PD173952



PD173956



PD173958



PD166326

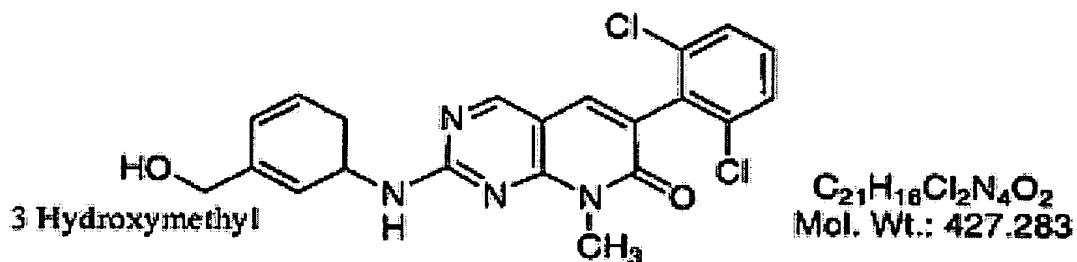
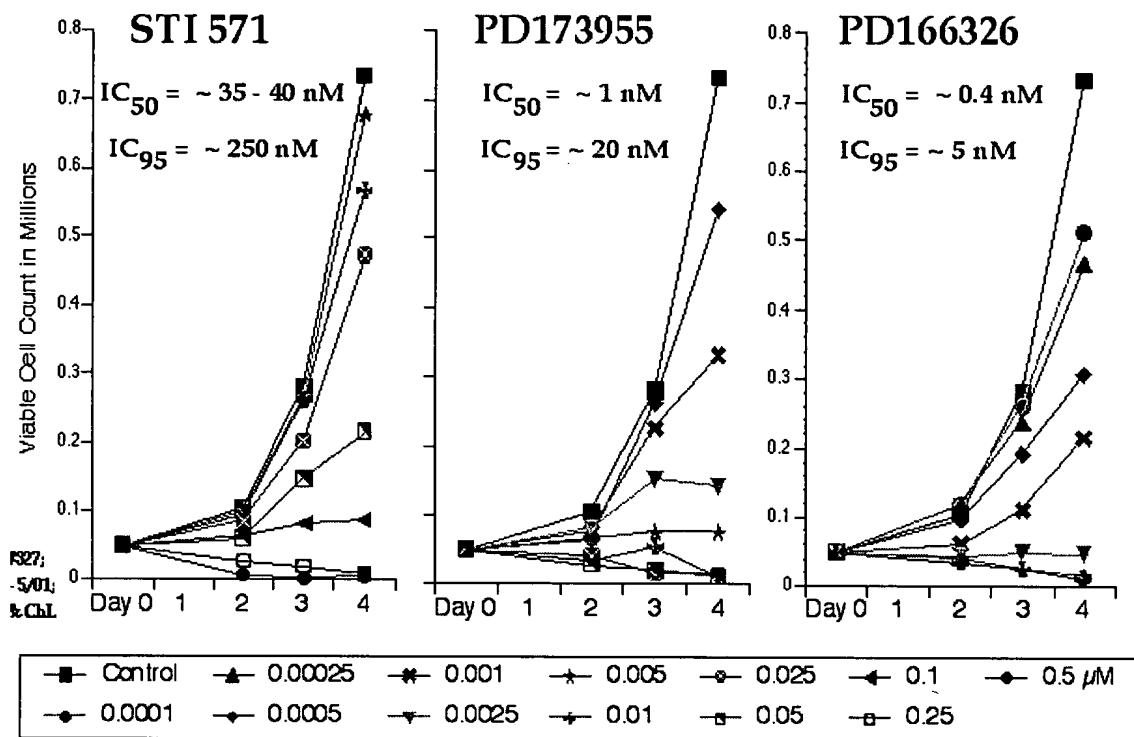


Figure 9

**Comparative Inhibition of Growth of R10 NEG Cells in Liquid Culture by STI571 (5 - 500 nM), PD173955 (0.5 - 50 nM), & PD166326 (0.1 - 10 nM)**



**Figure 10**

## Inhibition of $^3\text{H}$ -Tdr Uptake in Fresh Blast Cells from CML Patient in Blastic Phase by STI571, PD173955, & PD166326

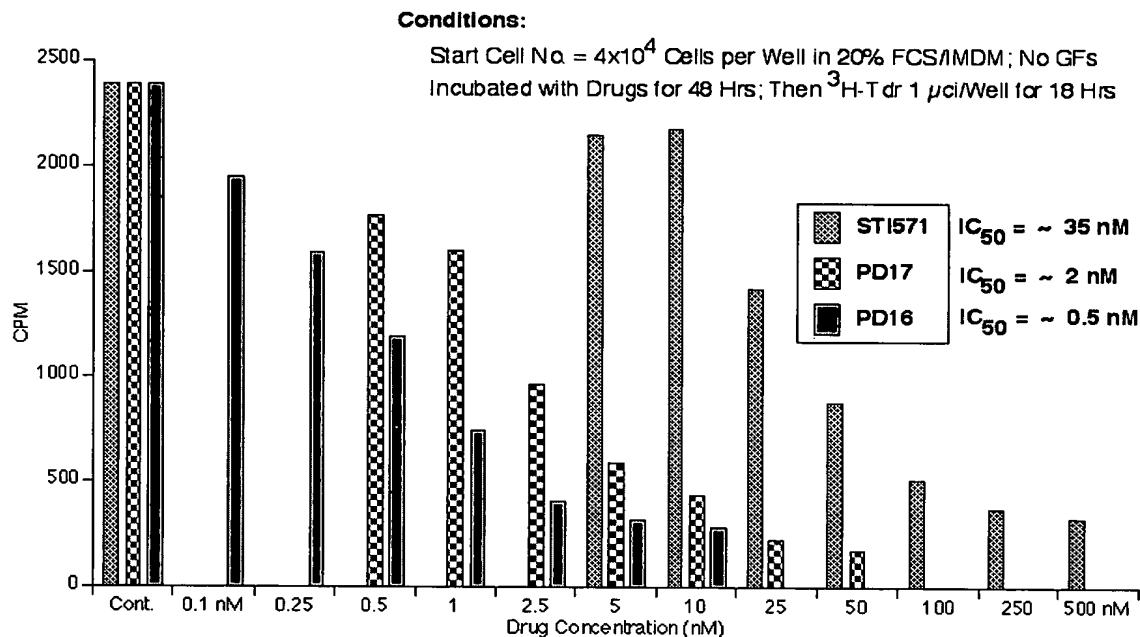


Figure 11

## Inhibition of $^3\text{H}$ -Tdr Uptake by Fresh Blast Cells with & without Cytokines from the Same CML Patient in Blastic Phase by STI571, PD173955, & PD166326

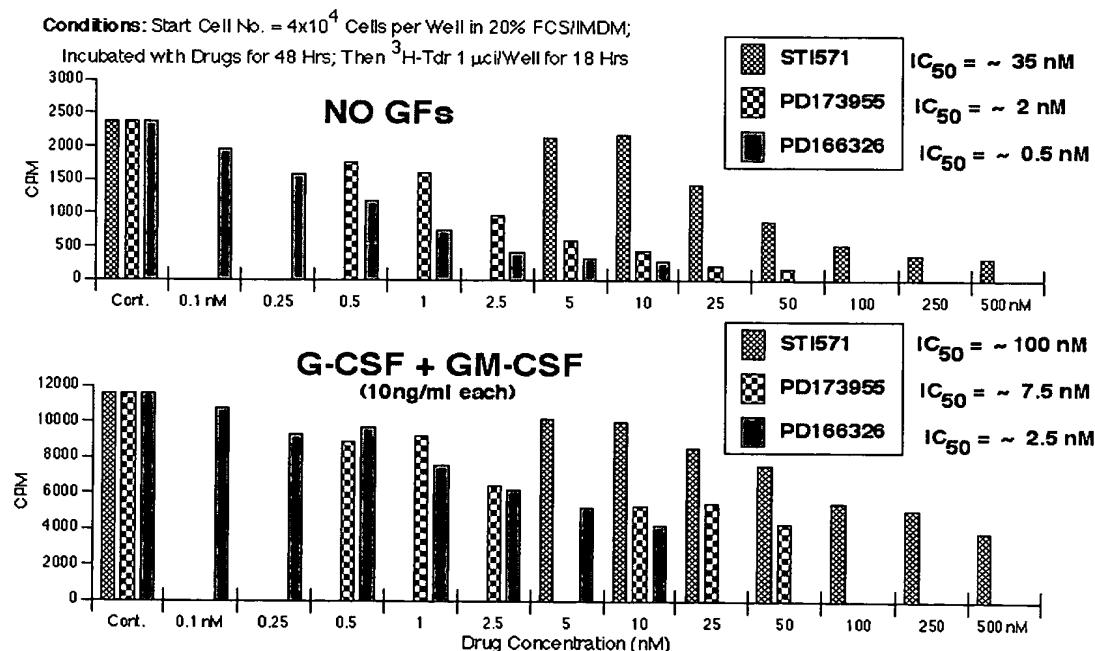


Figure 12

### Relative Sensitivity of Various Human Tumor Cell Lines to PD173955

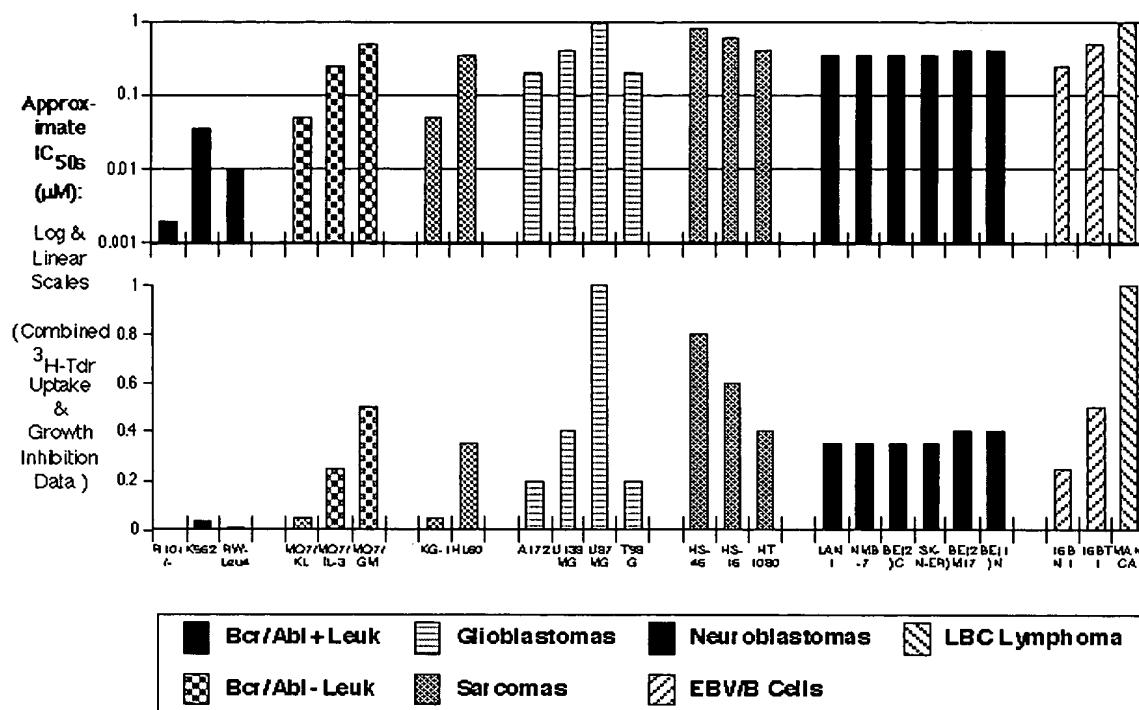


Figure 13

### Relative Sensitivity of Various Human Tumor Cell Lines to PD173955 & ST1571

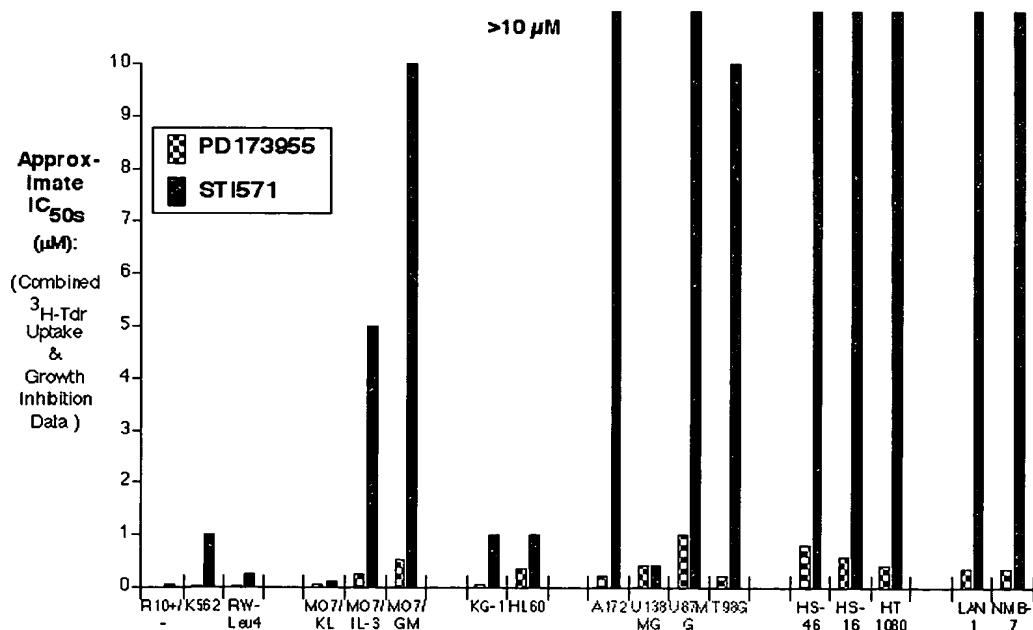
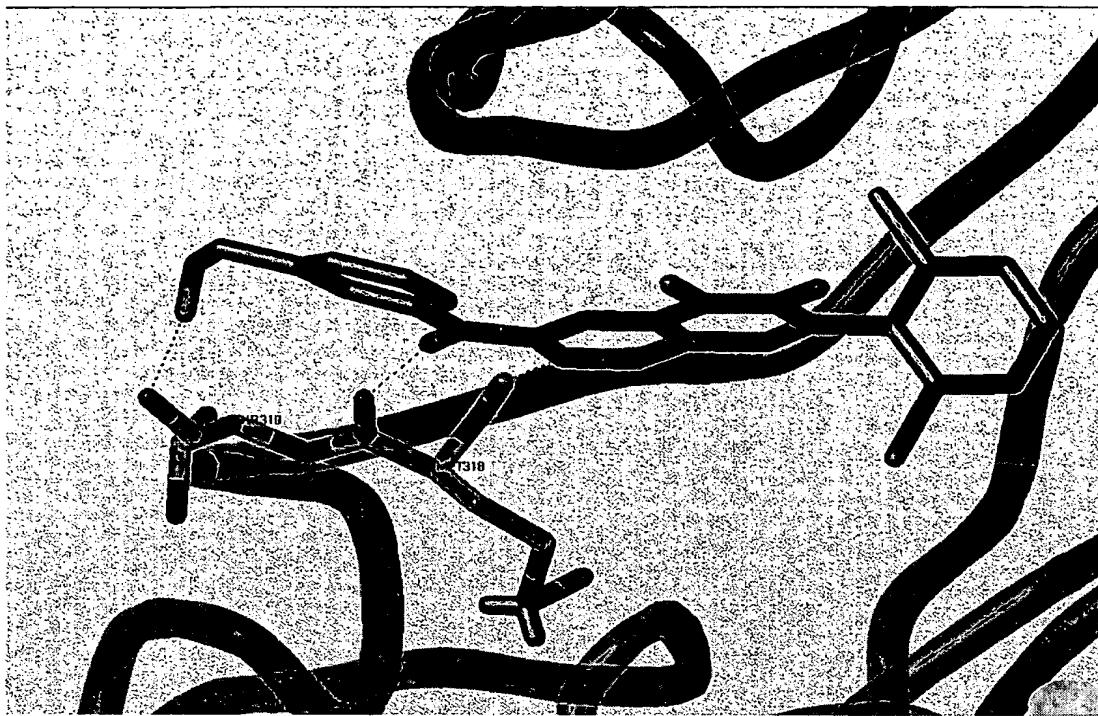


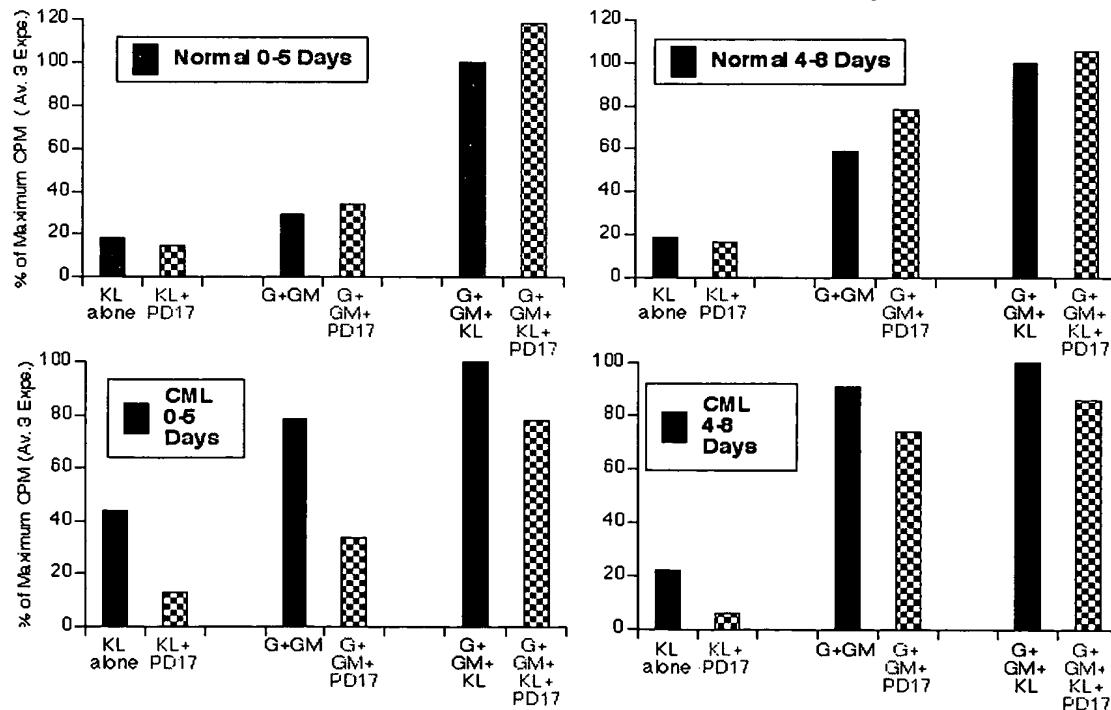
Figure 14

### PD 166326 binding to Abl Kinase (Modelled)



**Figure 15**

**10 nM PD173955 Inhibits Primary Early CML CD34+ GM Progenitors (0 - 5 Days) Substantially More than Later Maturing Progenitors (4 - 8 Days); No Inhibition of Comparable Normal Progenitors (Mean Values 3 Experiments)**



**Figure 16**

	IC50 (nM)	IC95-99 (nM)
PD166326	0.4	2.5
<b>SKI DV MO-16</b>	0.5	3.5
<b>SKI DV MO-17</b>	0.6	7.5
<b>SKI DV2 43</b>	0.8	7.5
<b>SKI DV1 10</b>	0.8	10
<b>Biotinyl SKI DV1 10</b>	1.5	10
<b>SKI DV2 47</b>	1.5	10
<b>SKI DV 115</b>	2	10
<b>SKI DV2 51</b>	2.5	15
<b>SKI DV2 87</b>	2.5	20
<b>SKI DV2 37</b>	7.5	50
<b>SKI DV2 53</b>	15	100
<b>SKI DV2 71</b>	20	200
<b>SKI DV2 35</b>	350	10000
<b>SKI DV2 33</b>	4000	>10000
<b>SKI DV 103</b>	10000	>10000

**Figure 17**

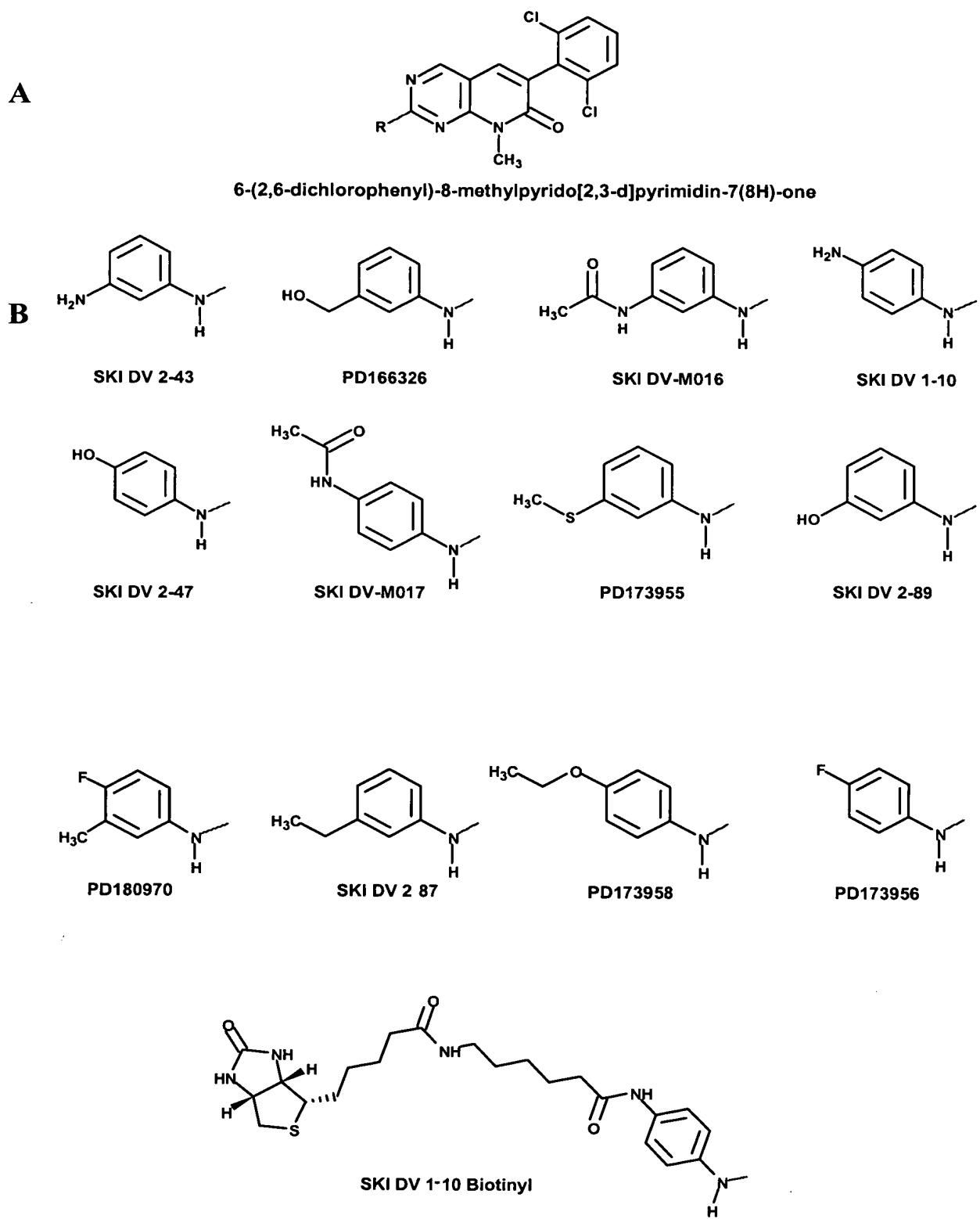
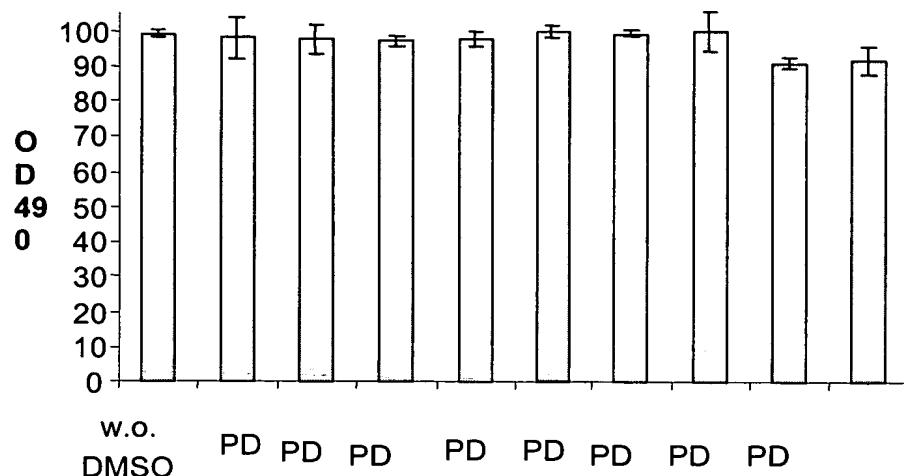
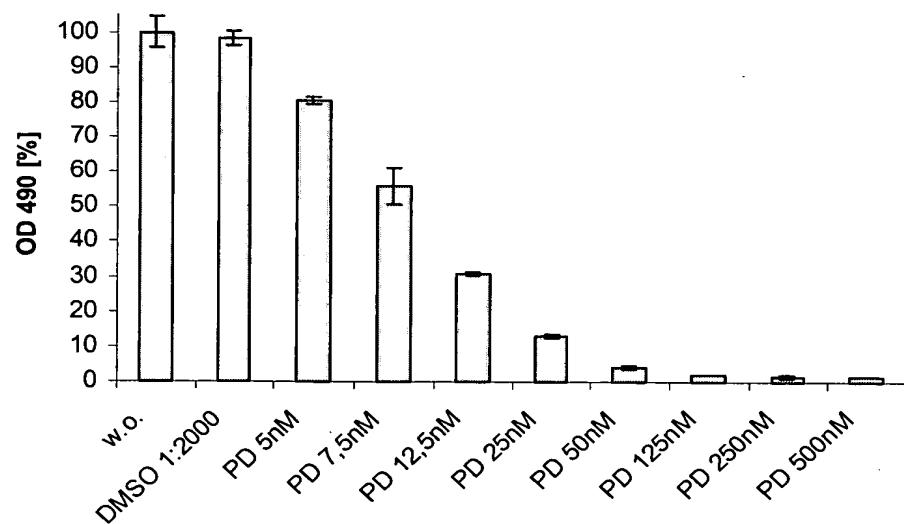
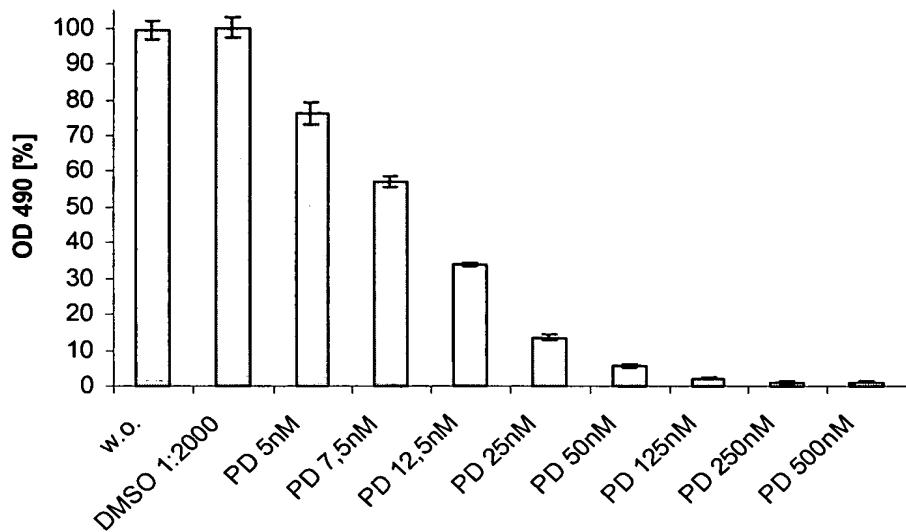
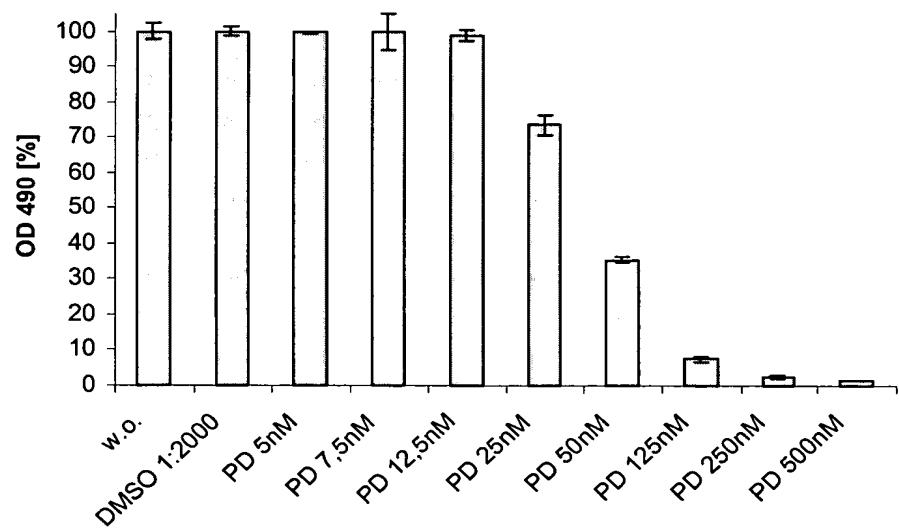


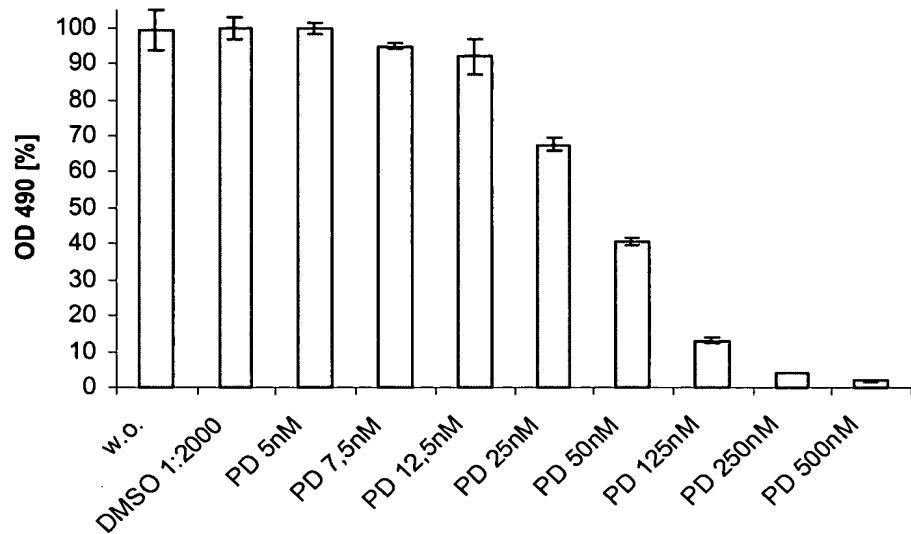
Figure 18

**A****PD166326 Ba/F3 par ntal****B****PD166326 Ba/F3 Bcr-Abl wild-type****Figure 19A**

**C****PD166326 Ba/F3 Bcr-Ab1 H396P****D****PD166326 Ba/F3 Bcr-Ab1 E255K****Figure 19B**

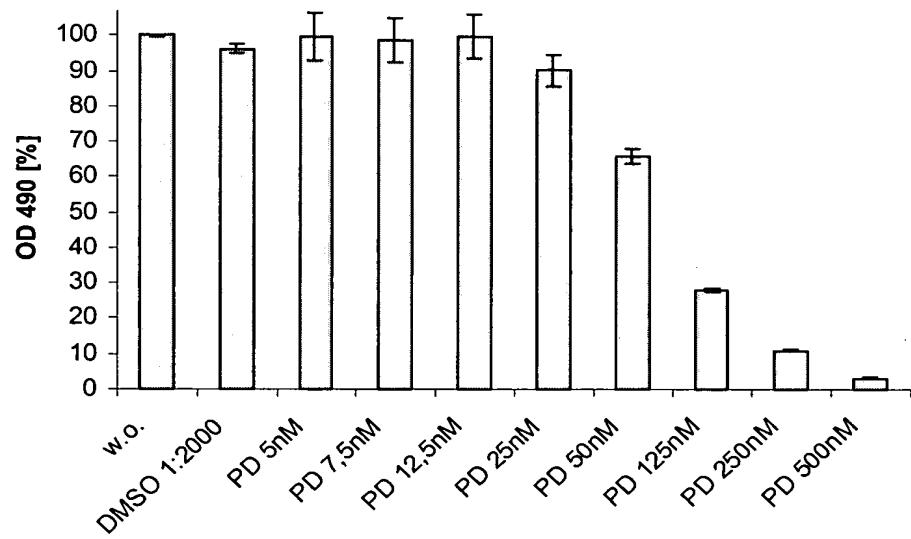
**E**

**PD166326 Ba/F3 Bcr-Ab1 Y253H**



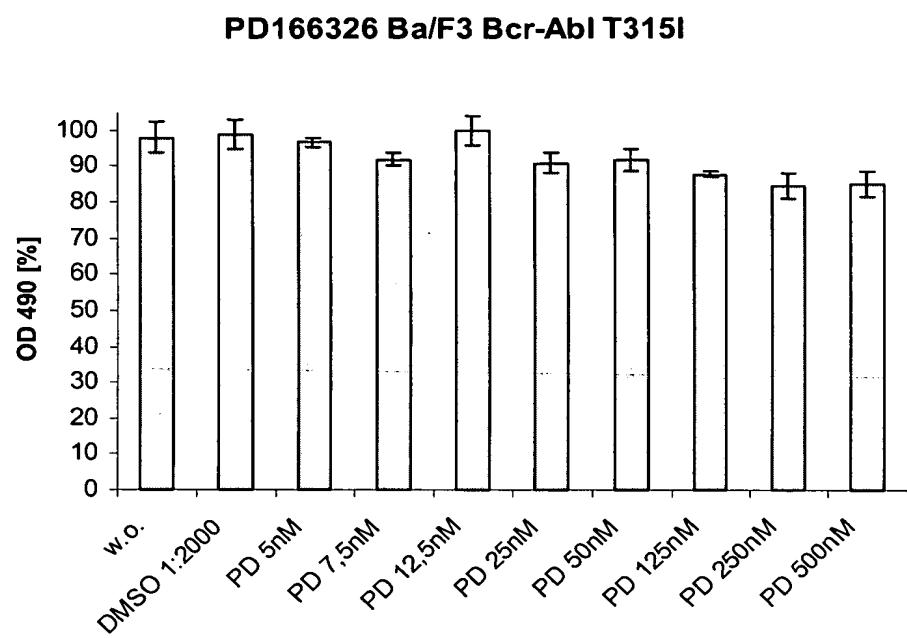
**F**

**PD166326 Ba/F3 Bcr-Ab1 E255V**

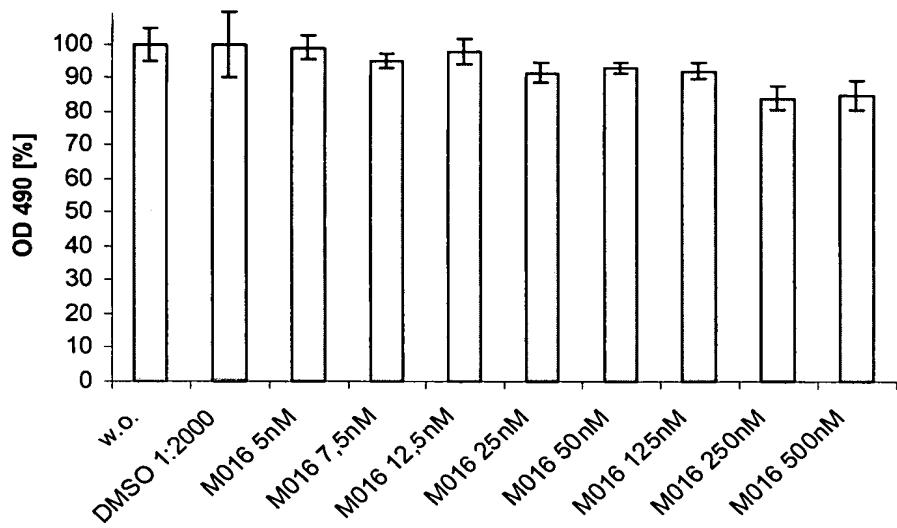
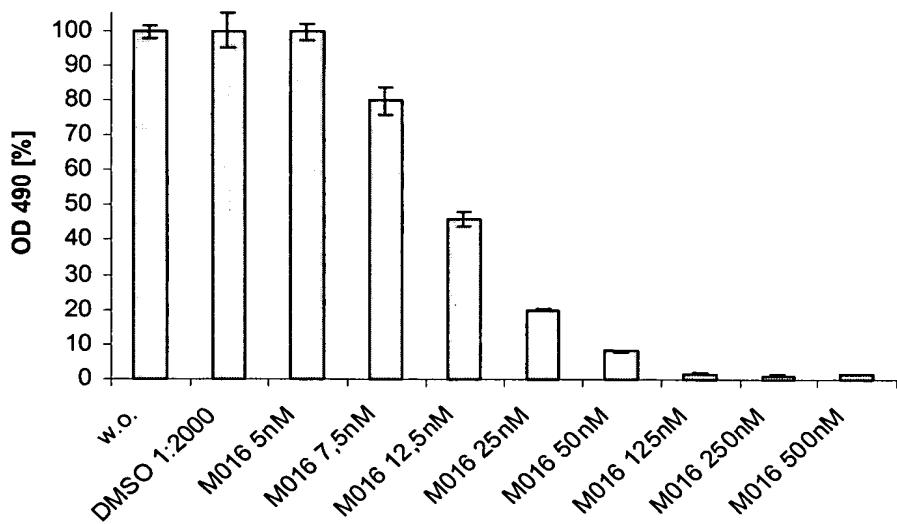


**Figure 19C**

**G**

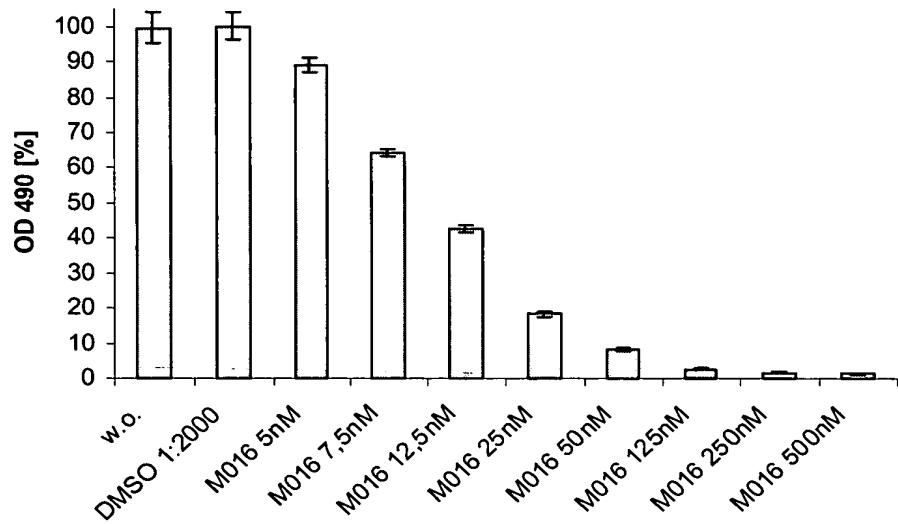


**Figure 19D**

**A****SKI DV-M016 Ba/F3 parental****B****SKI DV-M016 Ba/F3 Bcr-Abl wild-type****Figure 20A**

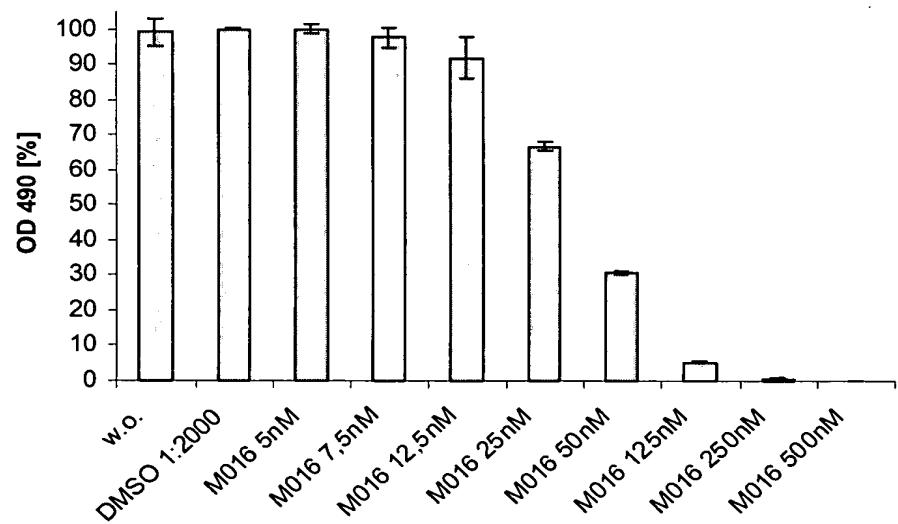
C

**SKI DV-M016 Ba/F3 Bcr-Abl H396P**



D

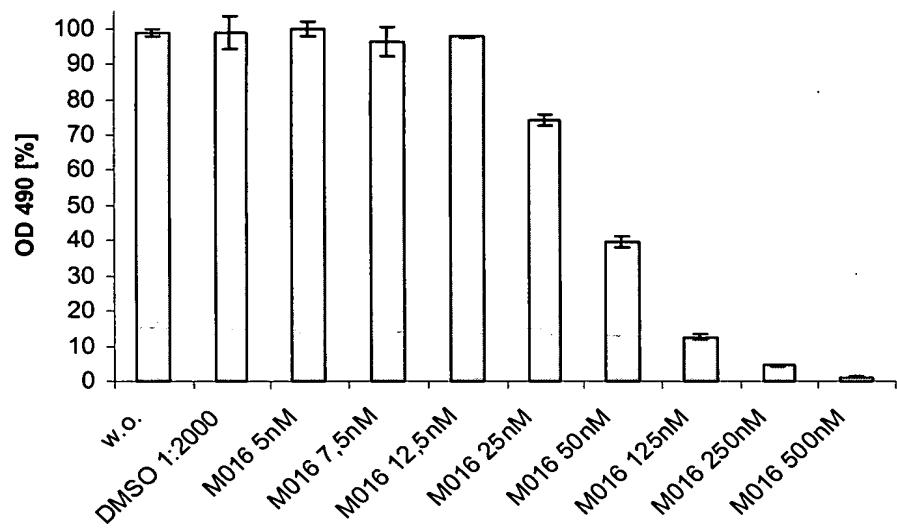
**SKI DV-M016 Ba/F3 Bcr-Abl E255K**



**Figure 20B**

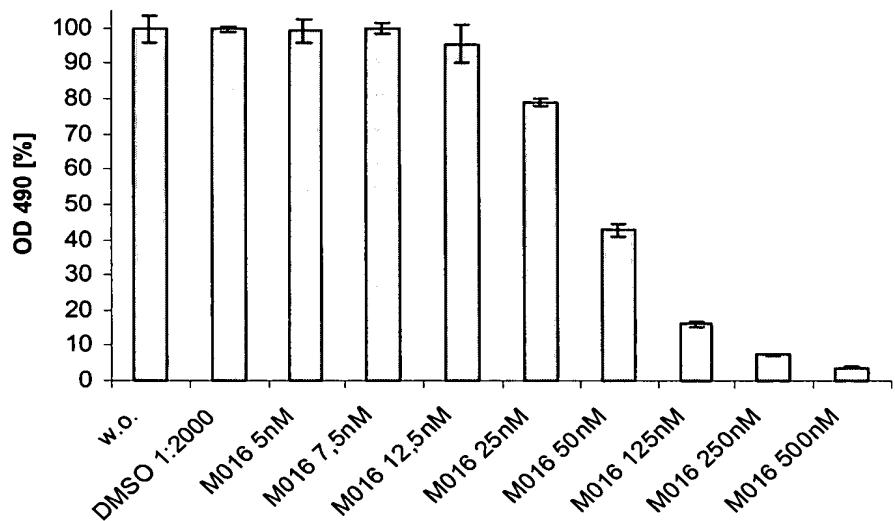
**E**

**SKI DV-M016 Ba/F3 Bcr-Abl Y253H**



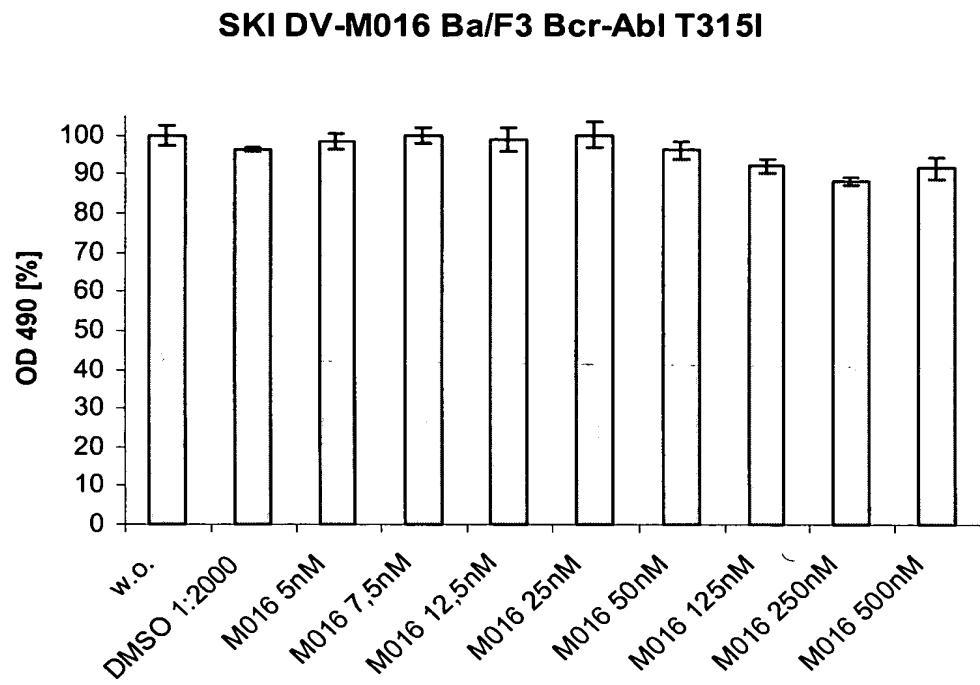
**F**

**SKI DV-M016 Ba/F3 Bcr-Abl E255V**

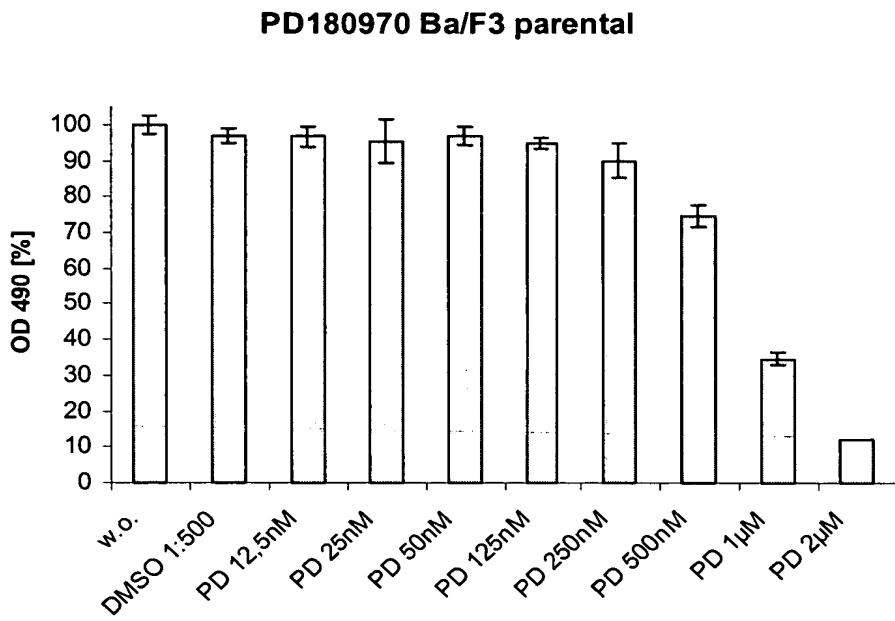
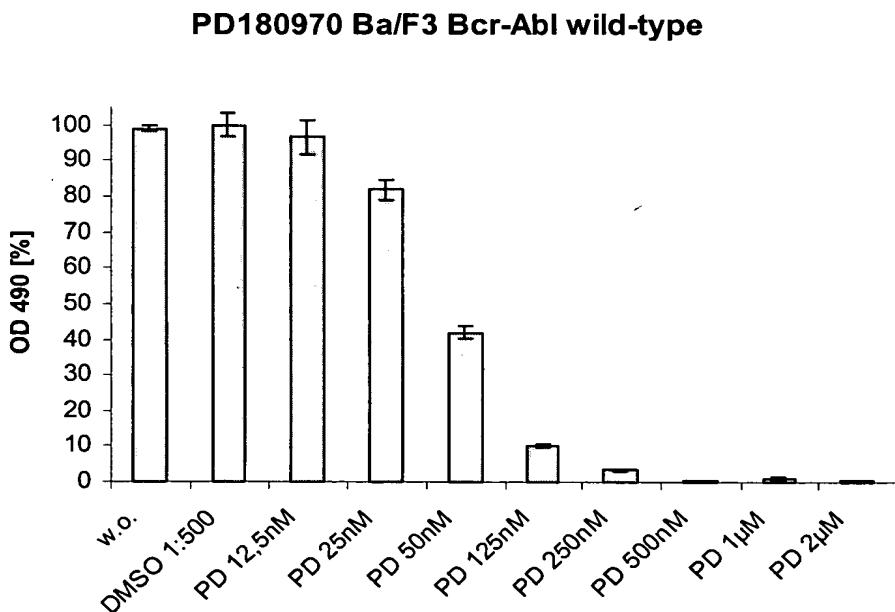


**Figure 20C**

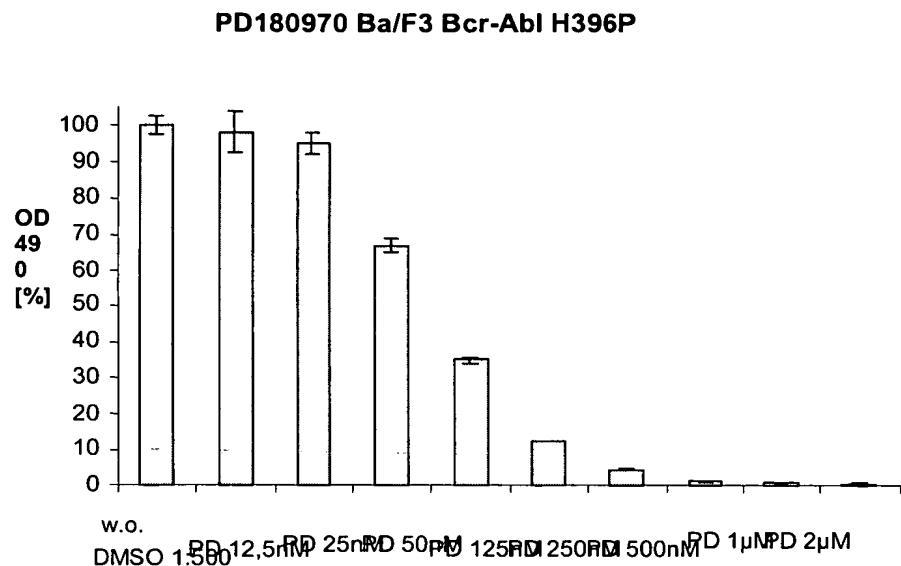
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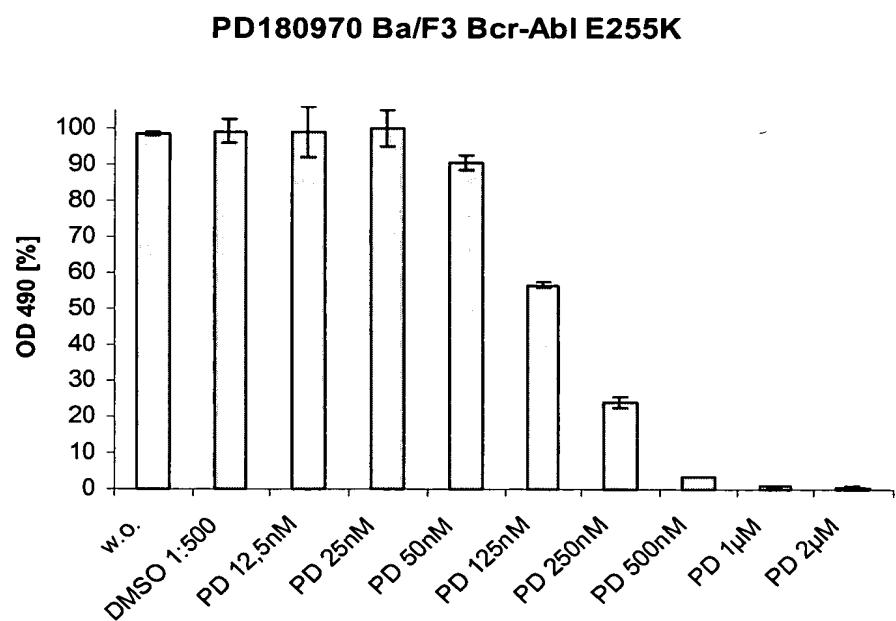
**Figure 20D**

**A****B****Figure 21A**

**C**



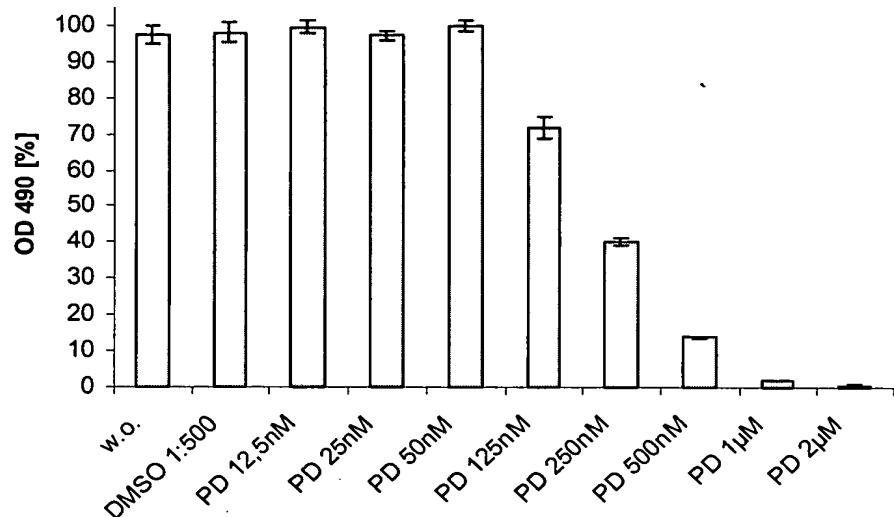
**D**



**Figure 21B**

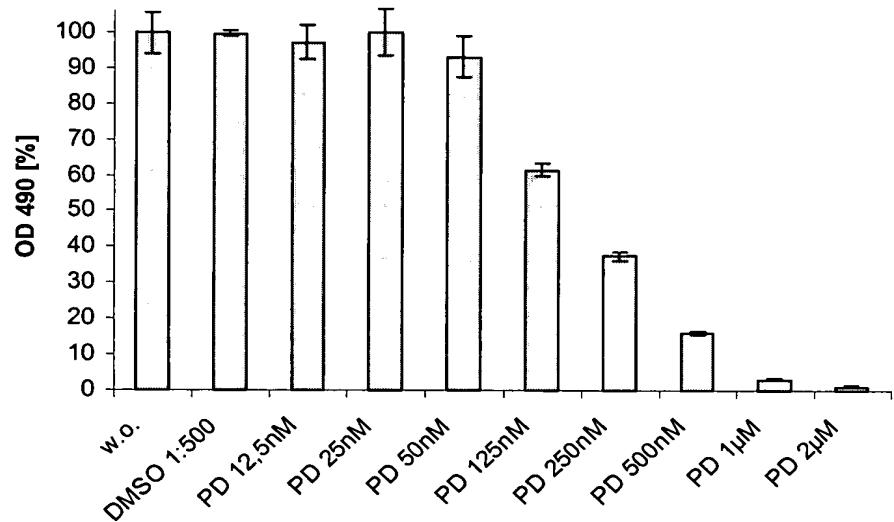
**E**

**PD180970 Ba/F3 Bcr-Ab1 Y253H**



**F**

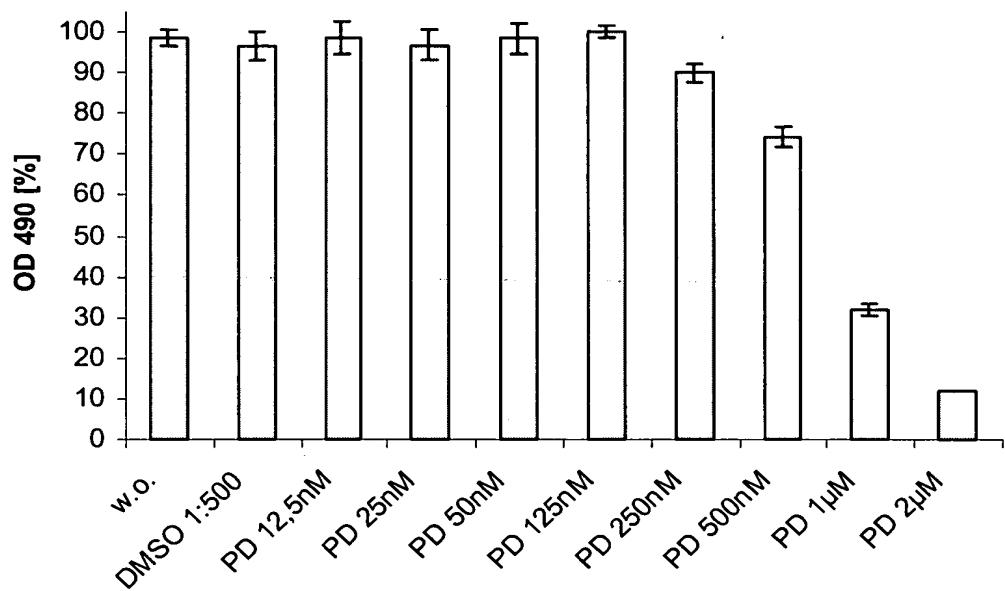
**PD180970 Ba/F3 Bcr-Ab1 E255V**



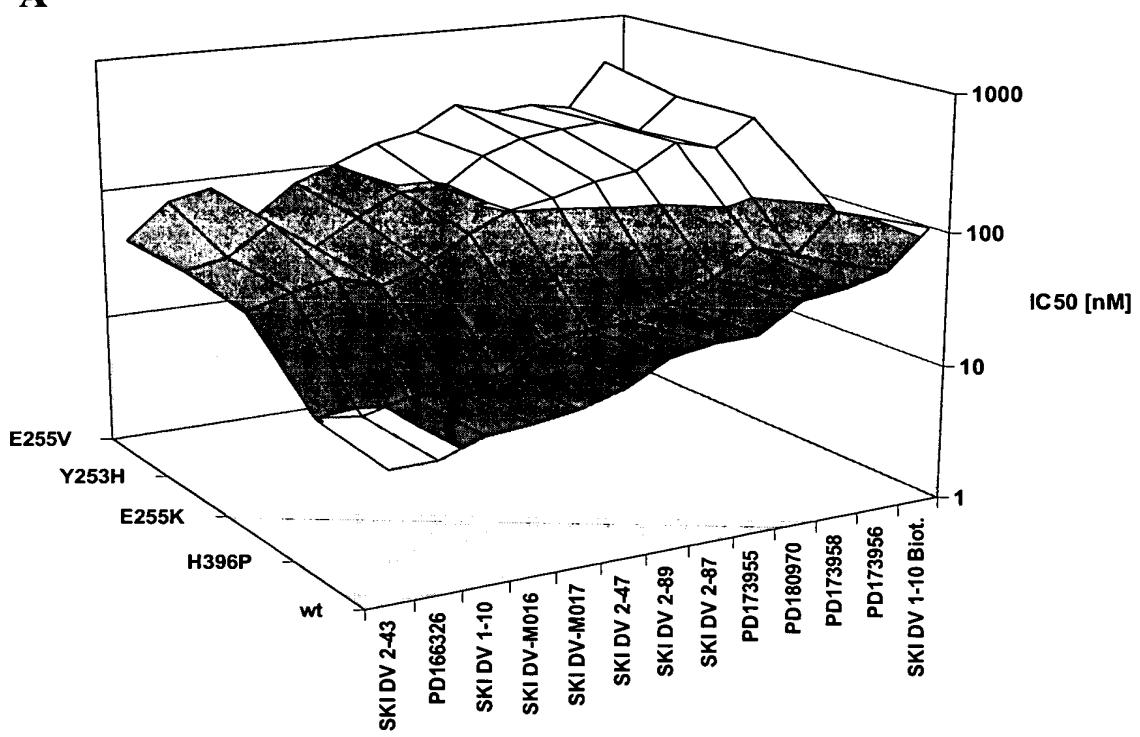
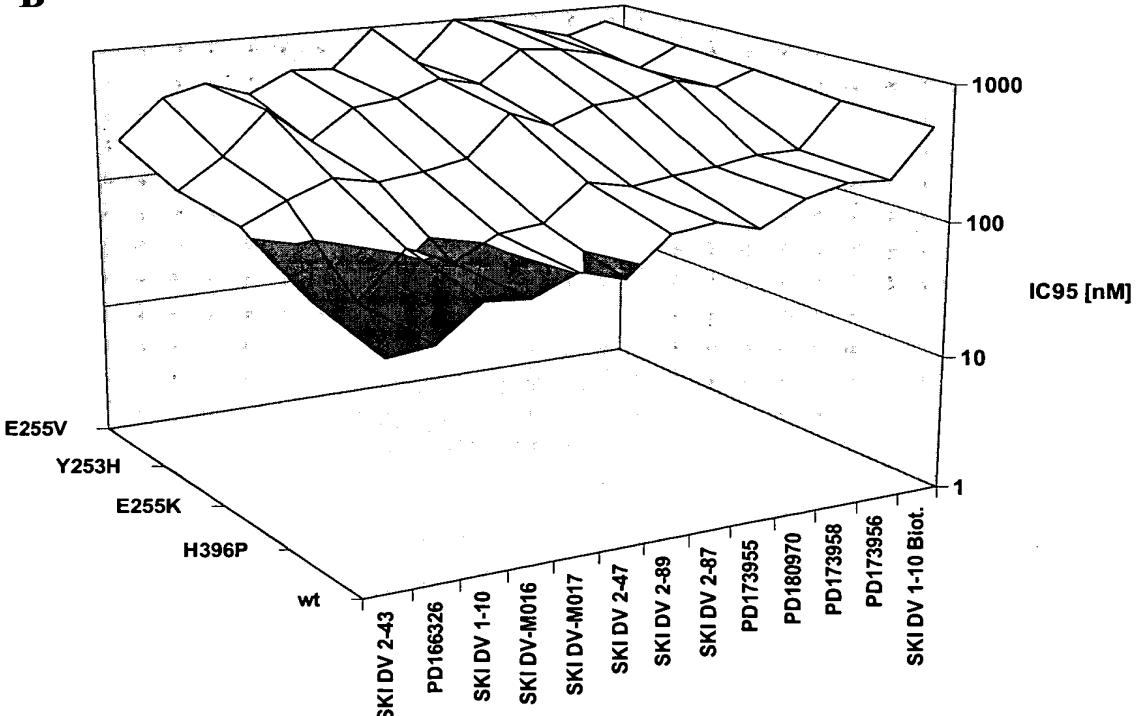
**Figure 21C**

**G**

**PD180970 Ba/F3 Bcr-Ab1 T315I**



**Figure 21D**

**A****B****Figure 22**

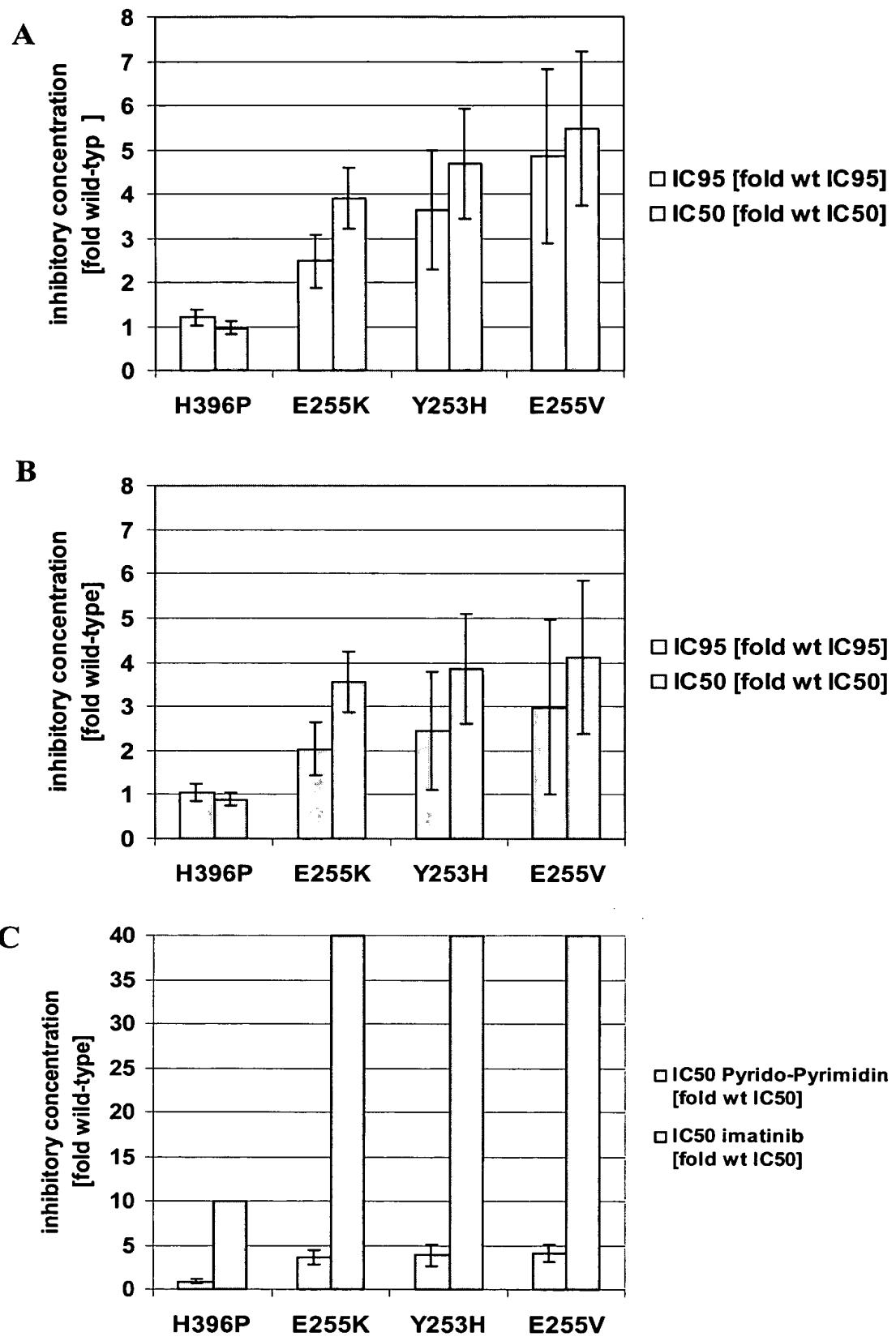


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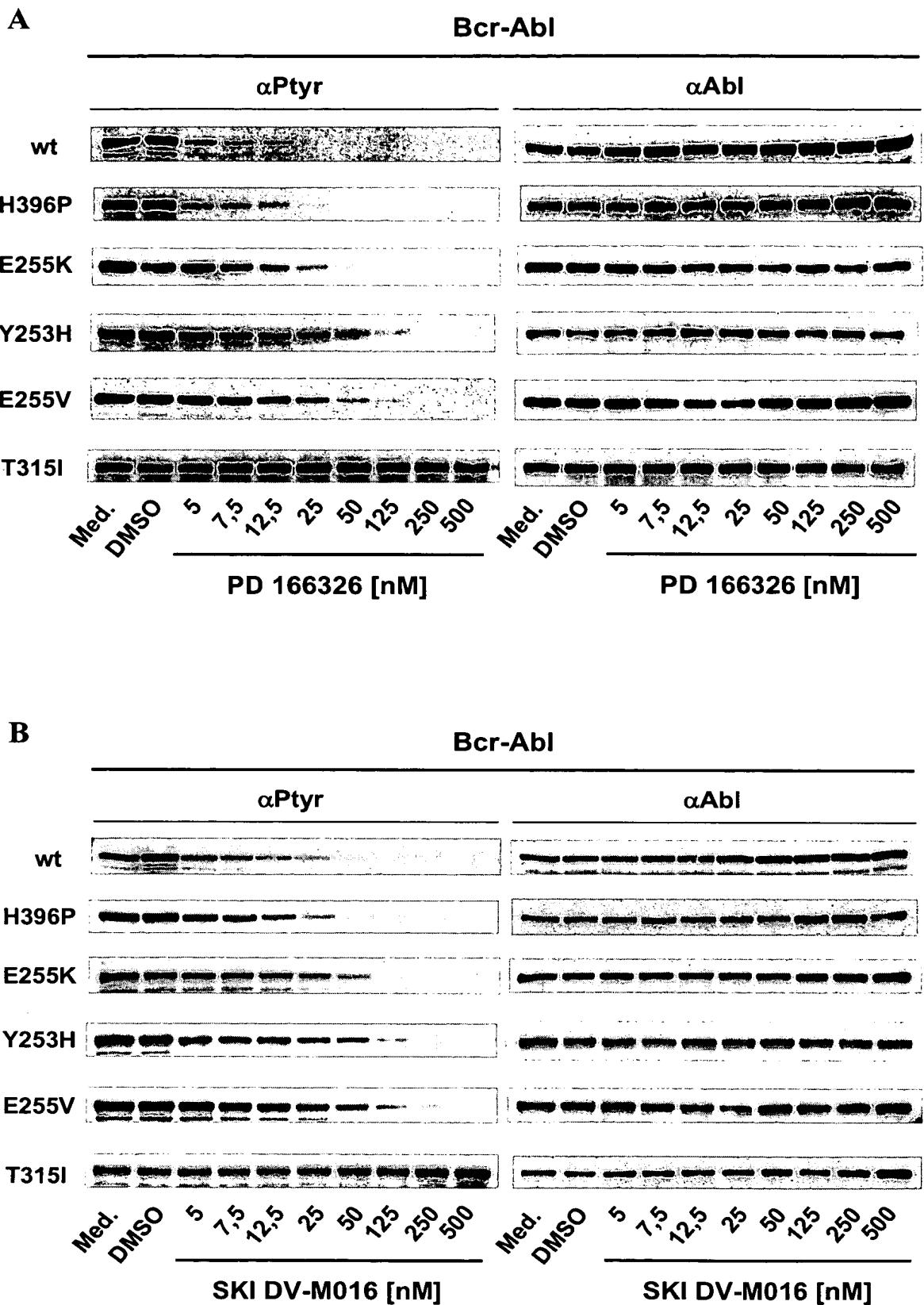
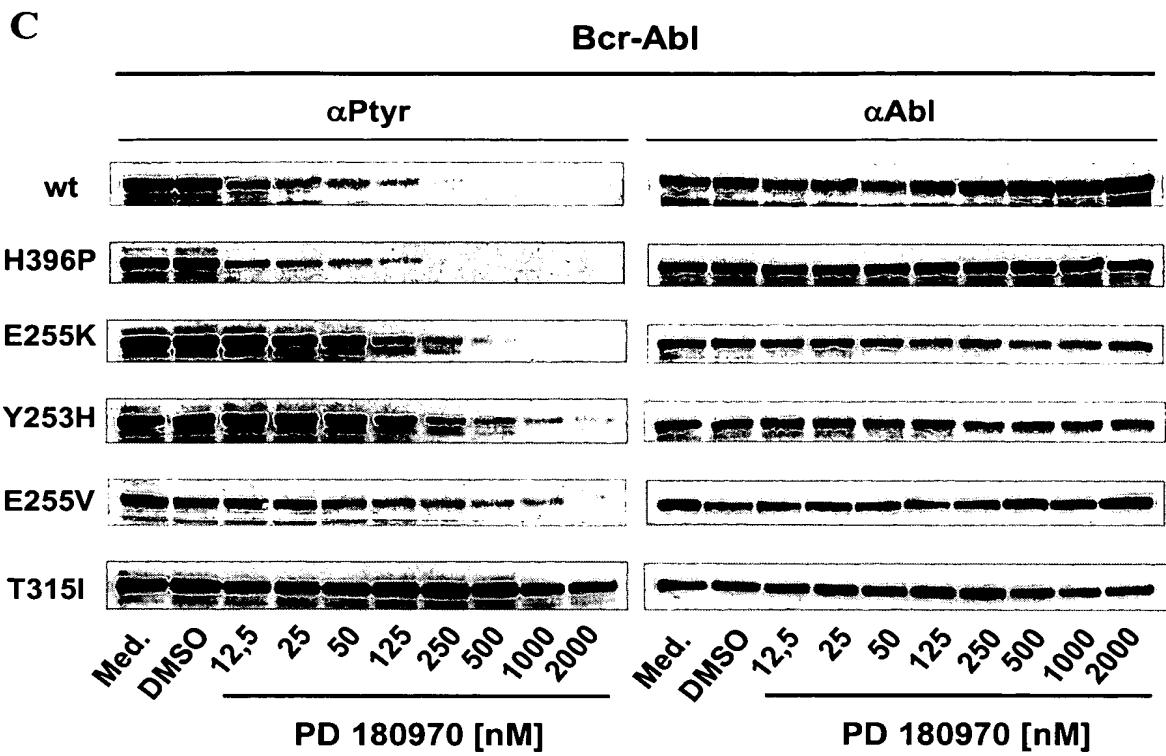
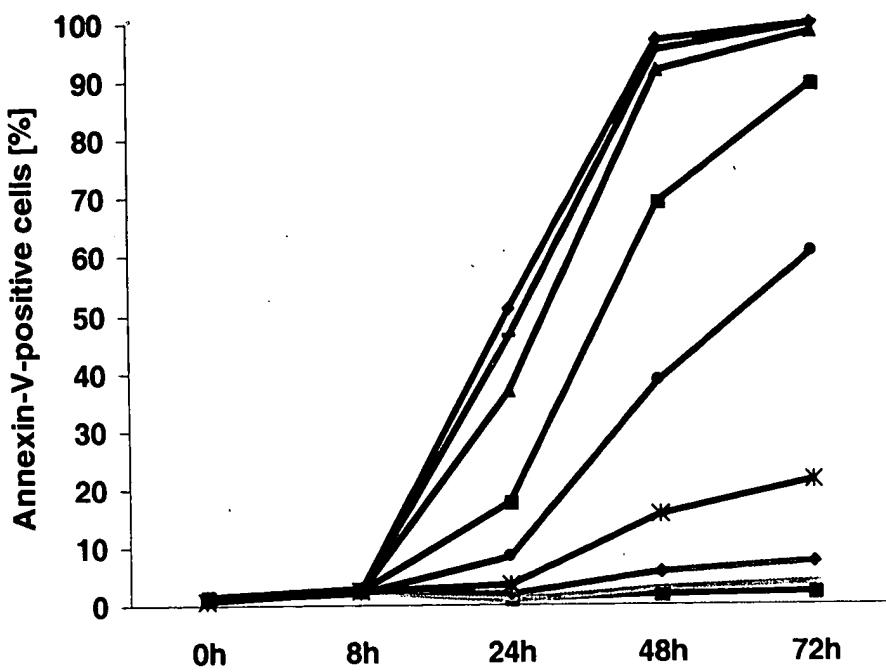
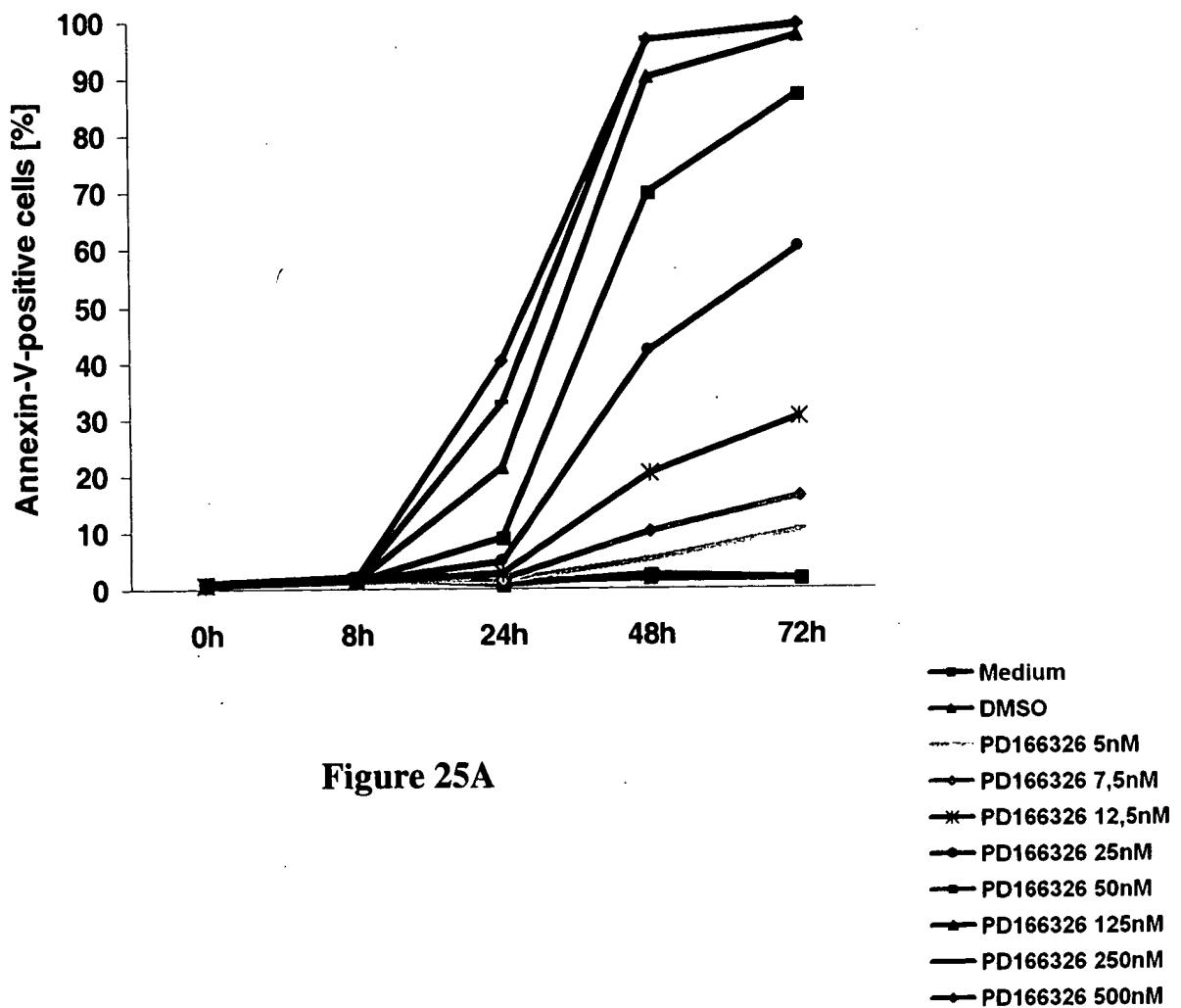
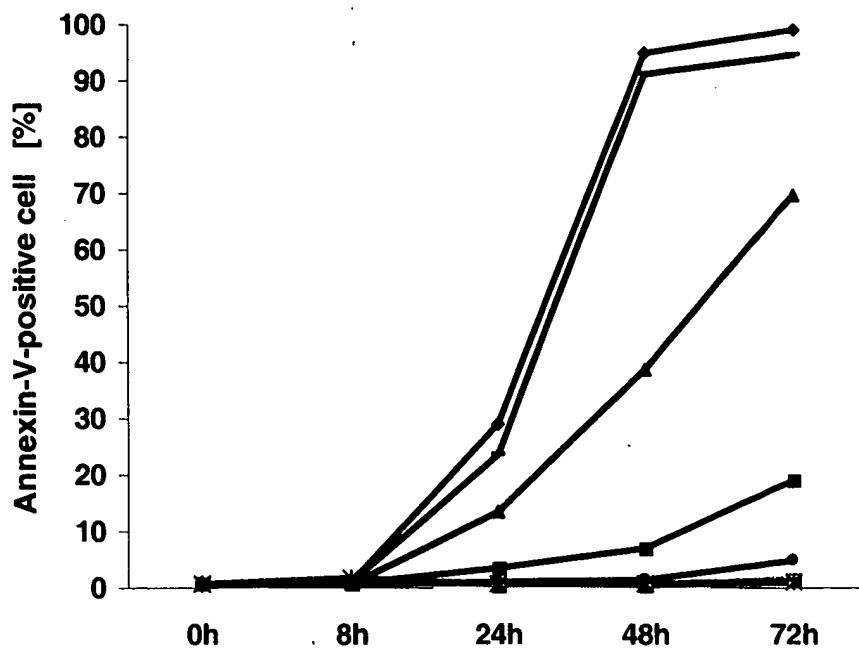
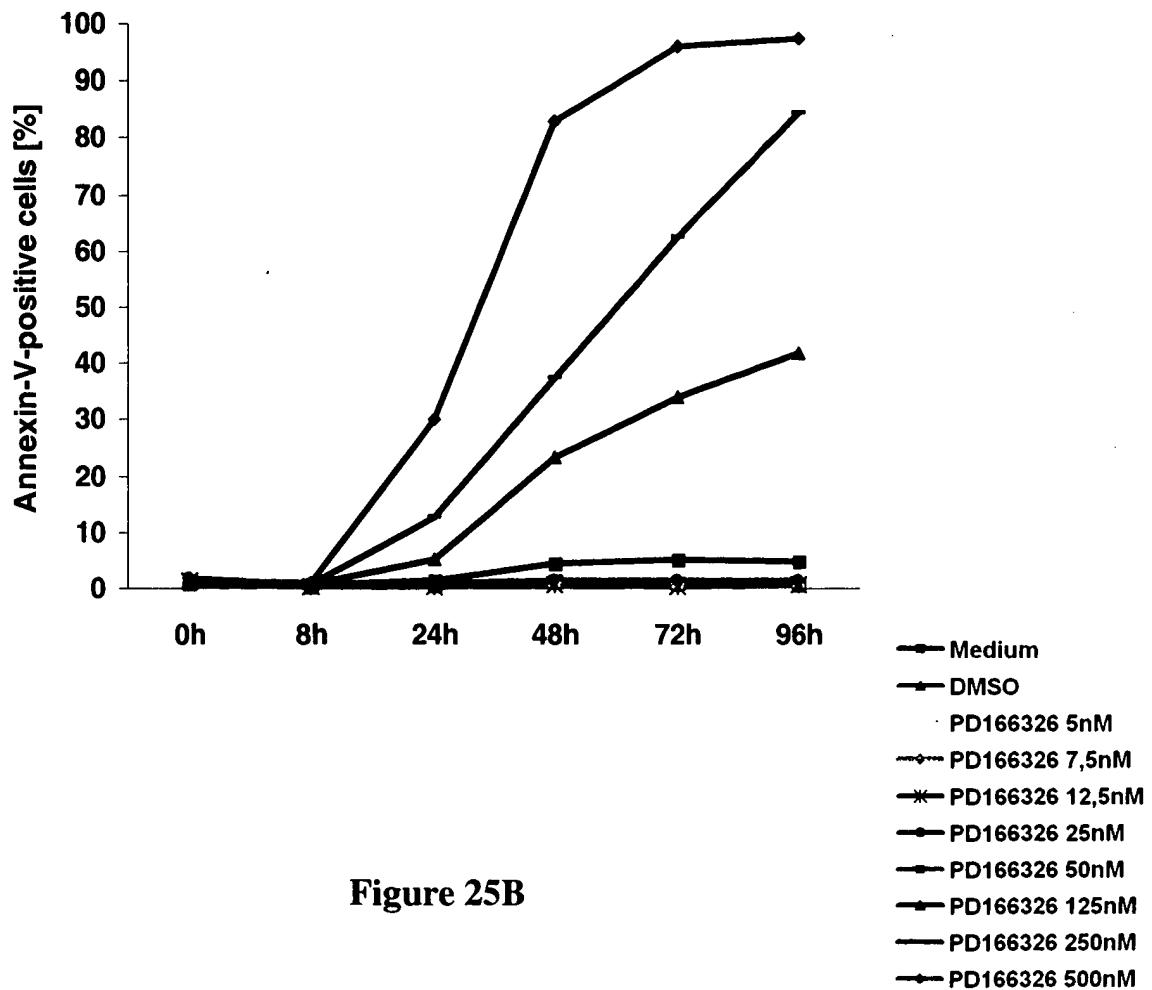


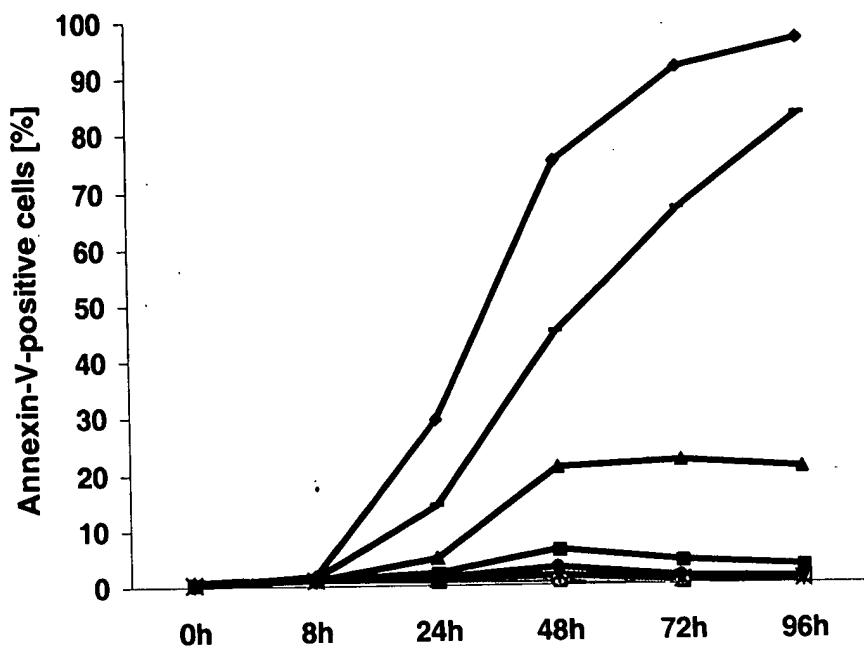
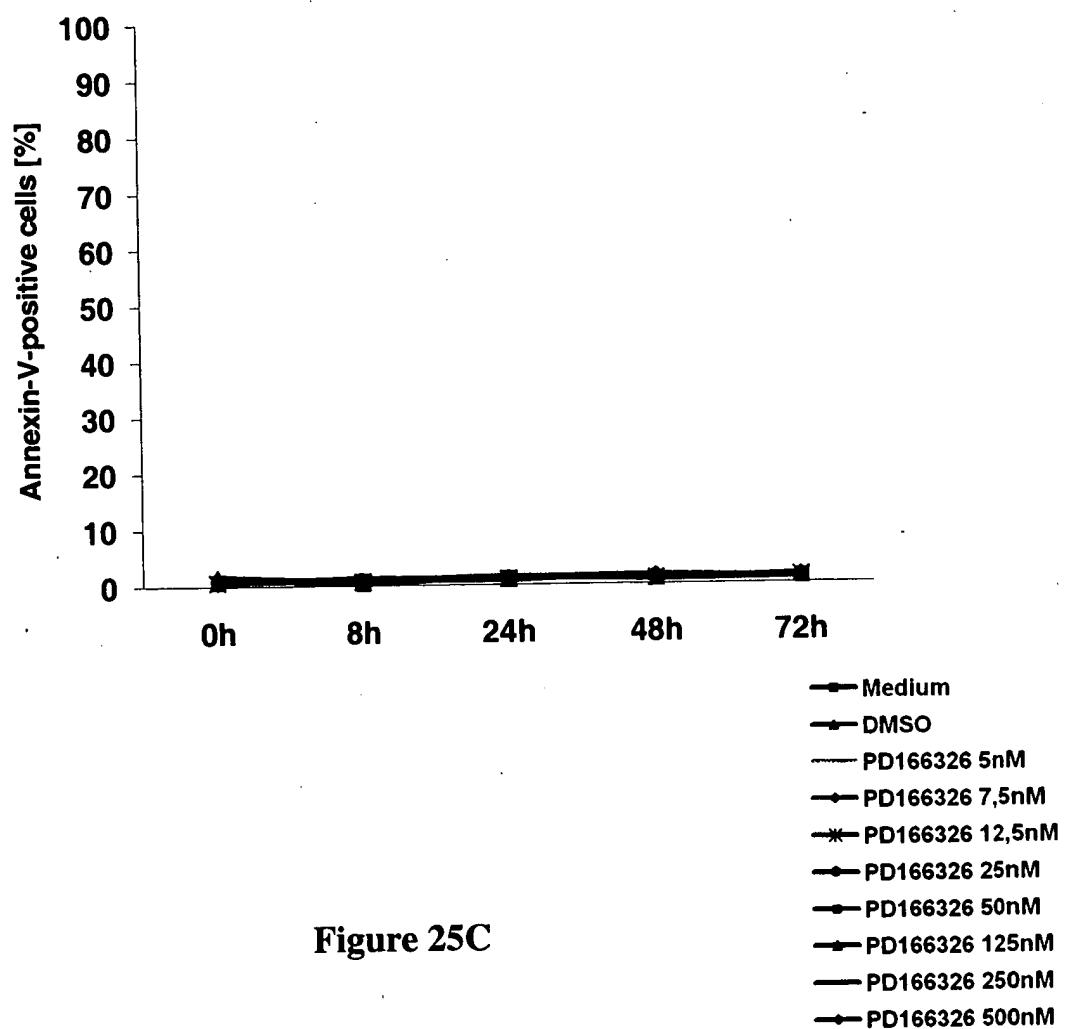
Figure 24



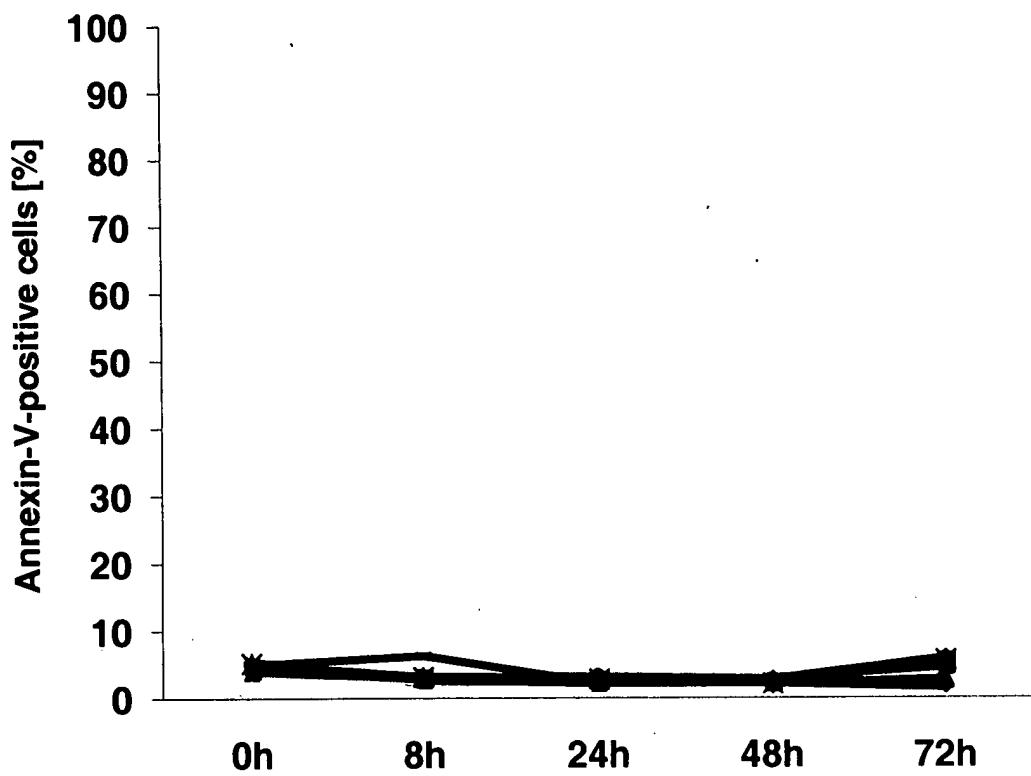
**Figure 24B**

**A****B****Figure 25A**

**C****D****Figure 25B**

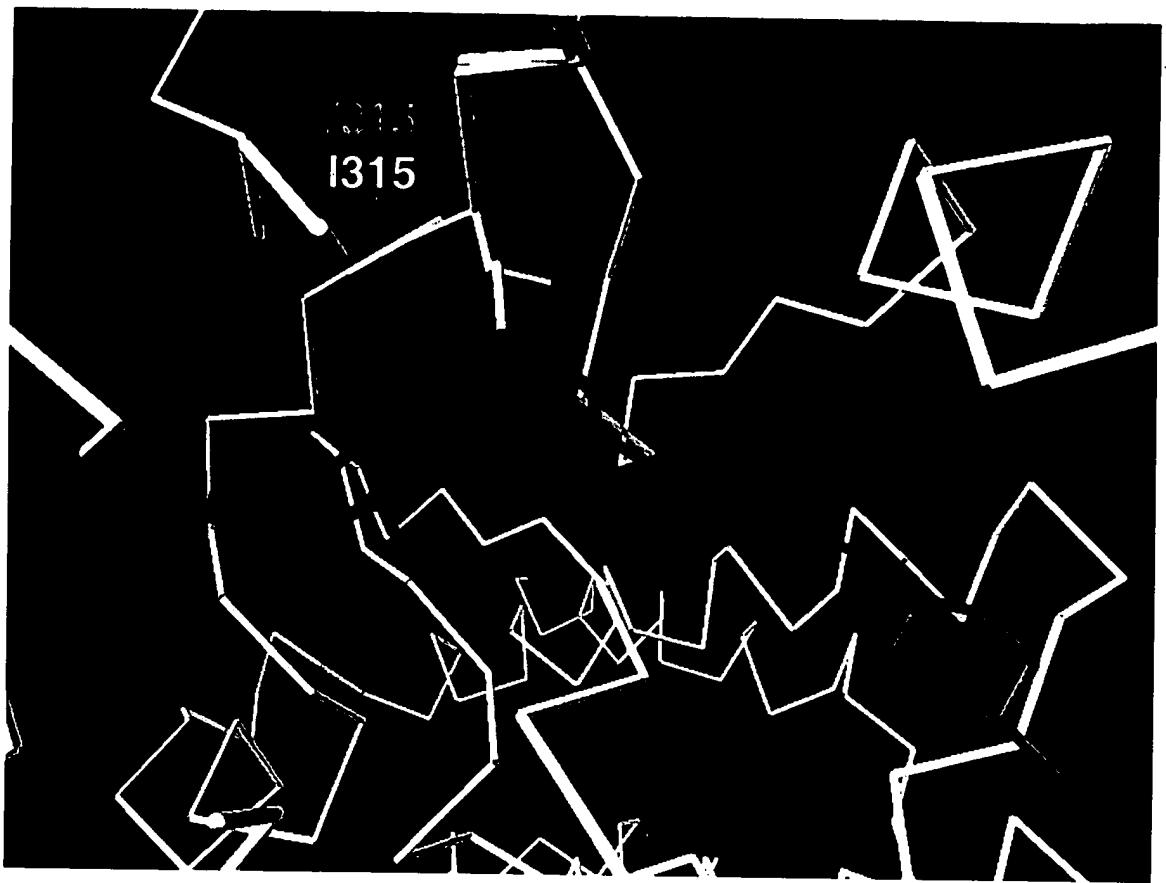
**E****F****Figure 25C**

**G**

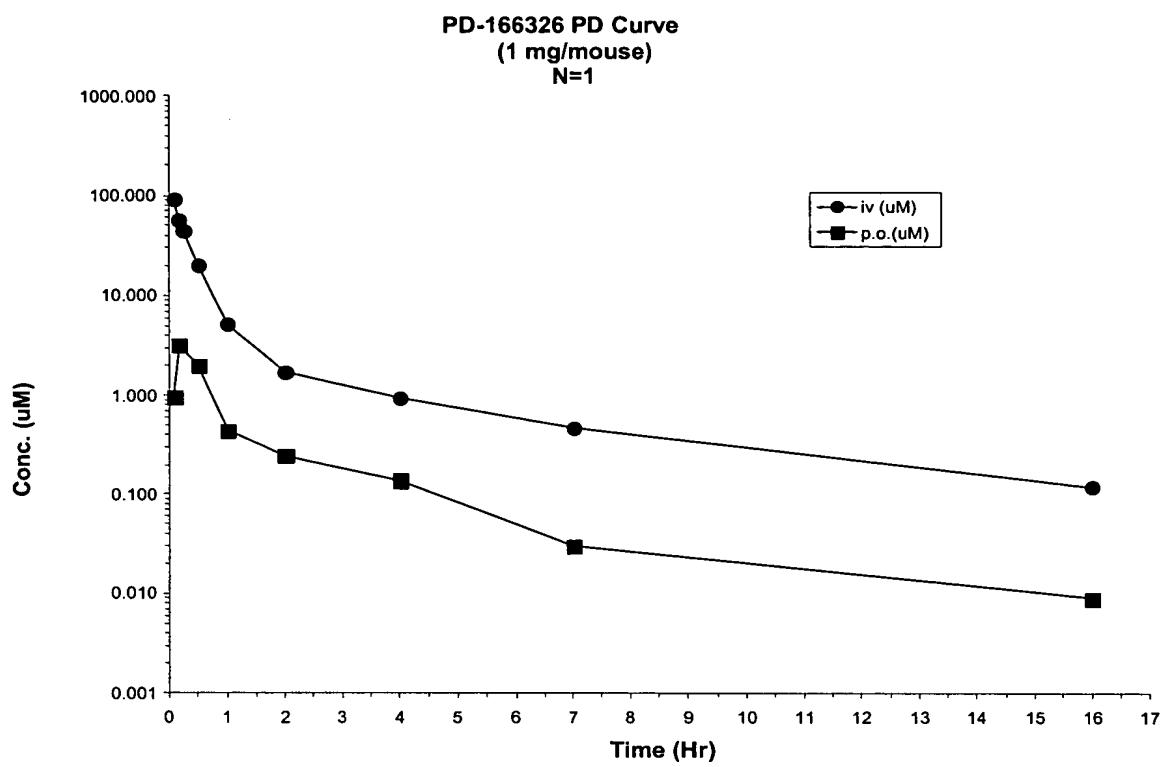


**Figure 25D**

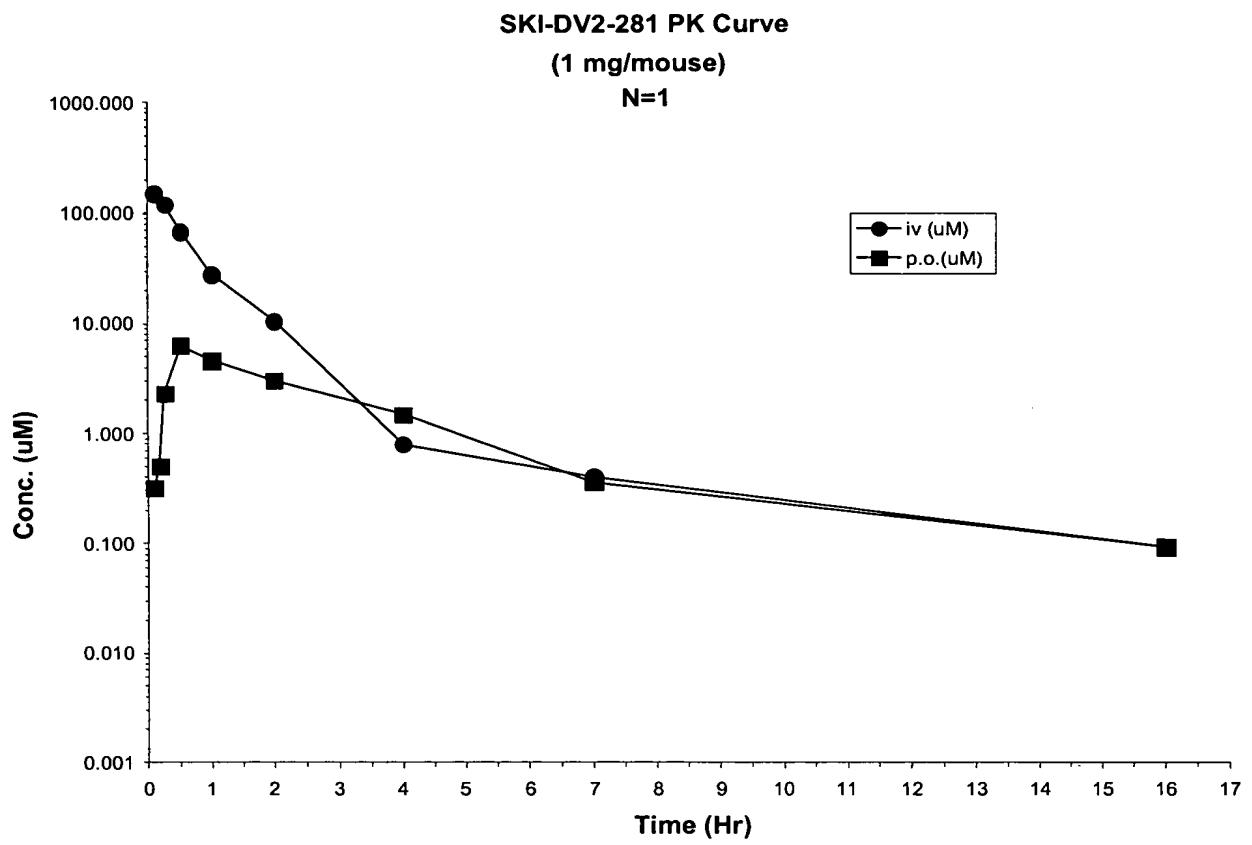
- Medium
- ▲— DMSO
- ◆— PD166326 5nM
- ◆— PD166326 7,5nM
- \*— PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- ▲— PD166326 125nM
- PD166326 250nM
- ◆— PD166326 500nM



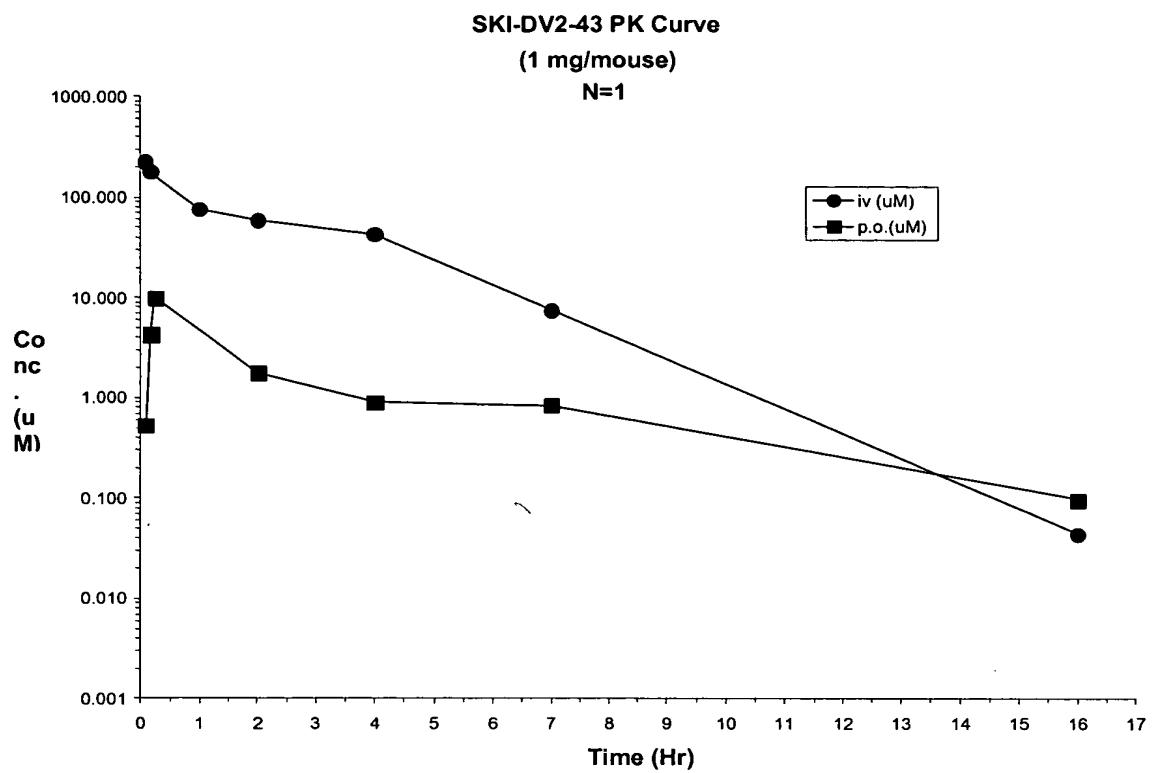
**Figure 26**



**Figure 27**

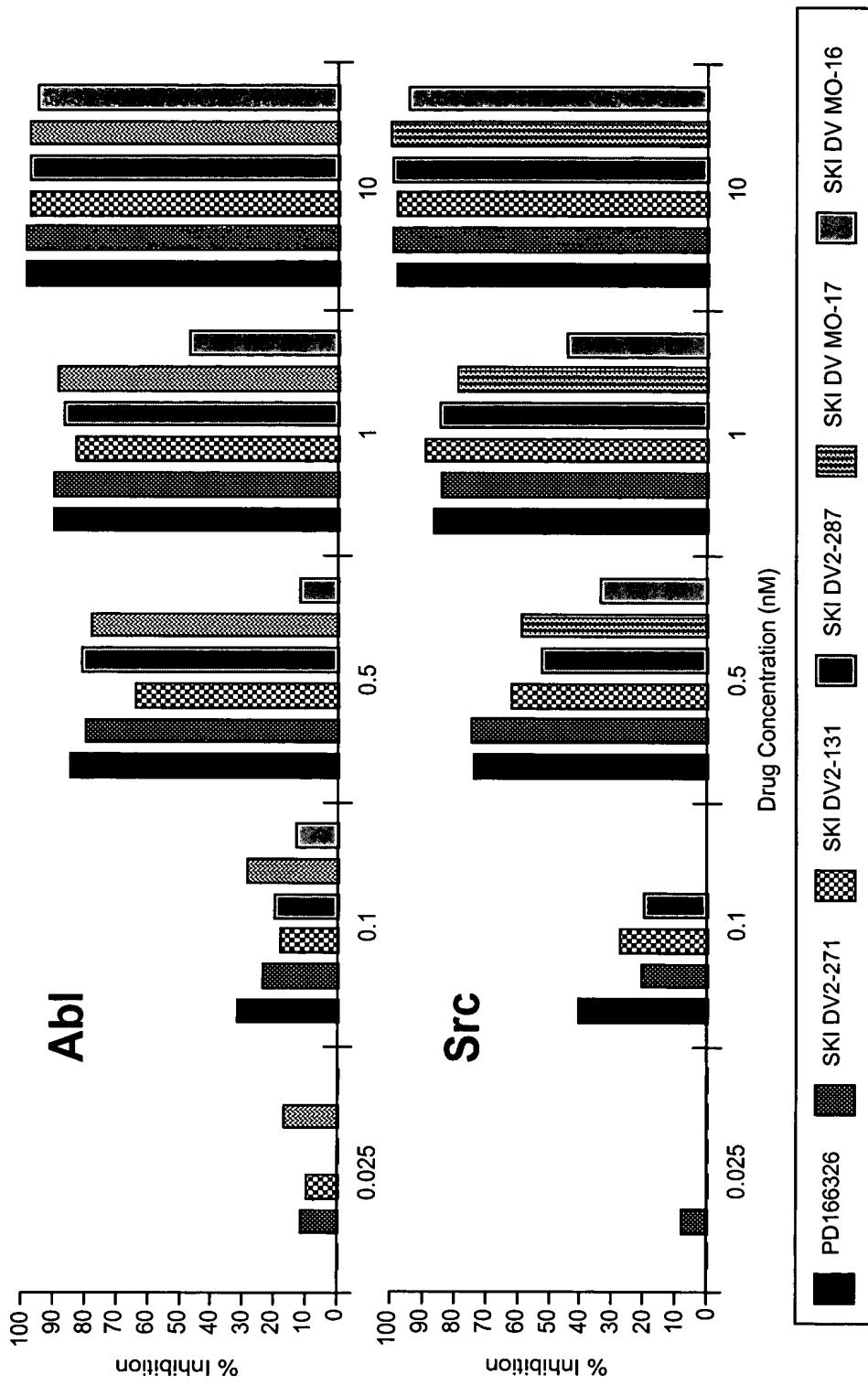


**Figure 28**



**Figure 29**

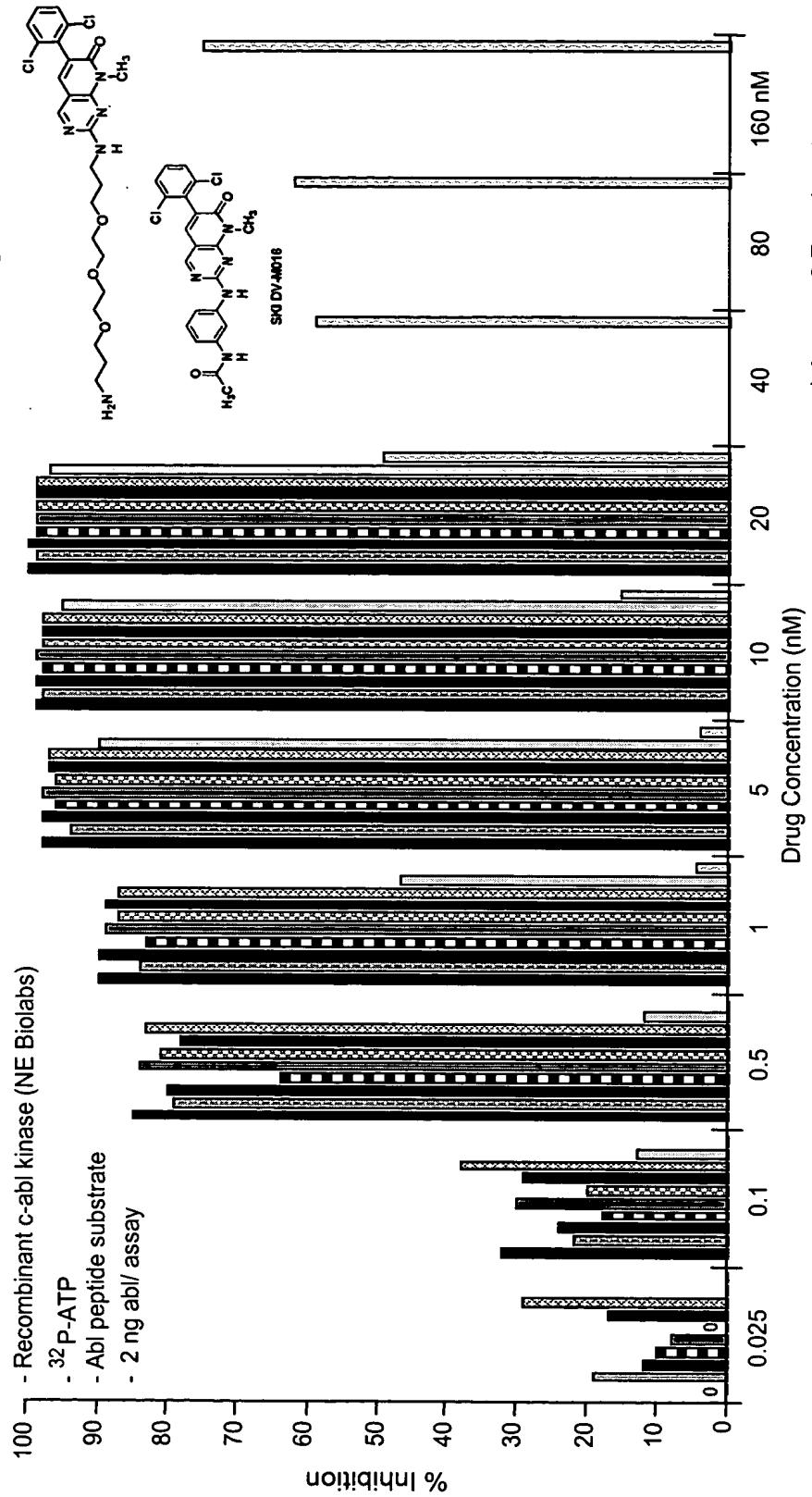
**Comparison of 6 of Most Inhibitory Pyrido-Pyrimidines to Bcr-Abl  
in Inhibiting Recombinant Abl & Src Kinases *in vitro***



**Figure 30**

**% Inhibition of Abl Protein Tyrosine Kinase Activity  
Compounds most Inhibitory in Cellular Assays +**

*invitro* by 8 Pyrido-pyrimidine  
PD173955 & SKI DV2 153



\* Average 2 Experiments

PD166326 *	SKI DV2-271 *	SKI DV2-43	SKI DV MO-17 *	SKI DV MO-16 *
PD179355 *	SKI DV2-131 *	SKI DV2-287 *	SKI DV 1-10	SKI DV2-153 *

Figure 31